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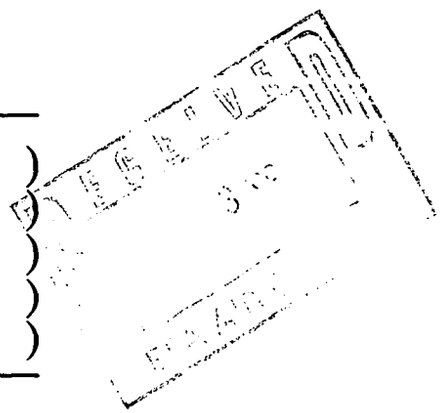
BEFORE THE
UNITED STATES
ENVIRONMENTAL PROTECTION AGENCY

IN RE APPLICATION FOR A FUEL ADDITIVE WAIVER FILED BY ETHYL CORPORATION UNDER § 211 (f) (4) OF THE CLEAN AIR ACT	)))))



APPENDICES TO COMMENTS IN SUPPORT OF THE WAIVER APPLICATION FOR THE HiTEC 3000 PERFORMANCE ADDITIVE

VOLUME TWO

APPENDICES 4, 5, 6, 7, 8, 9, 10 AND 11

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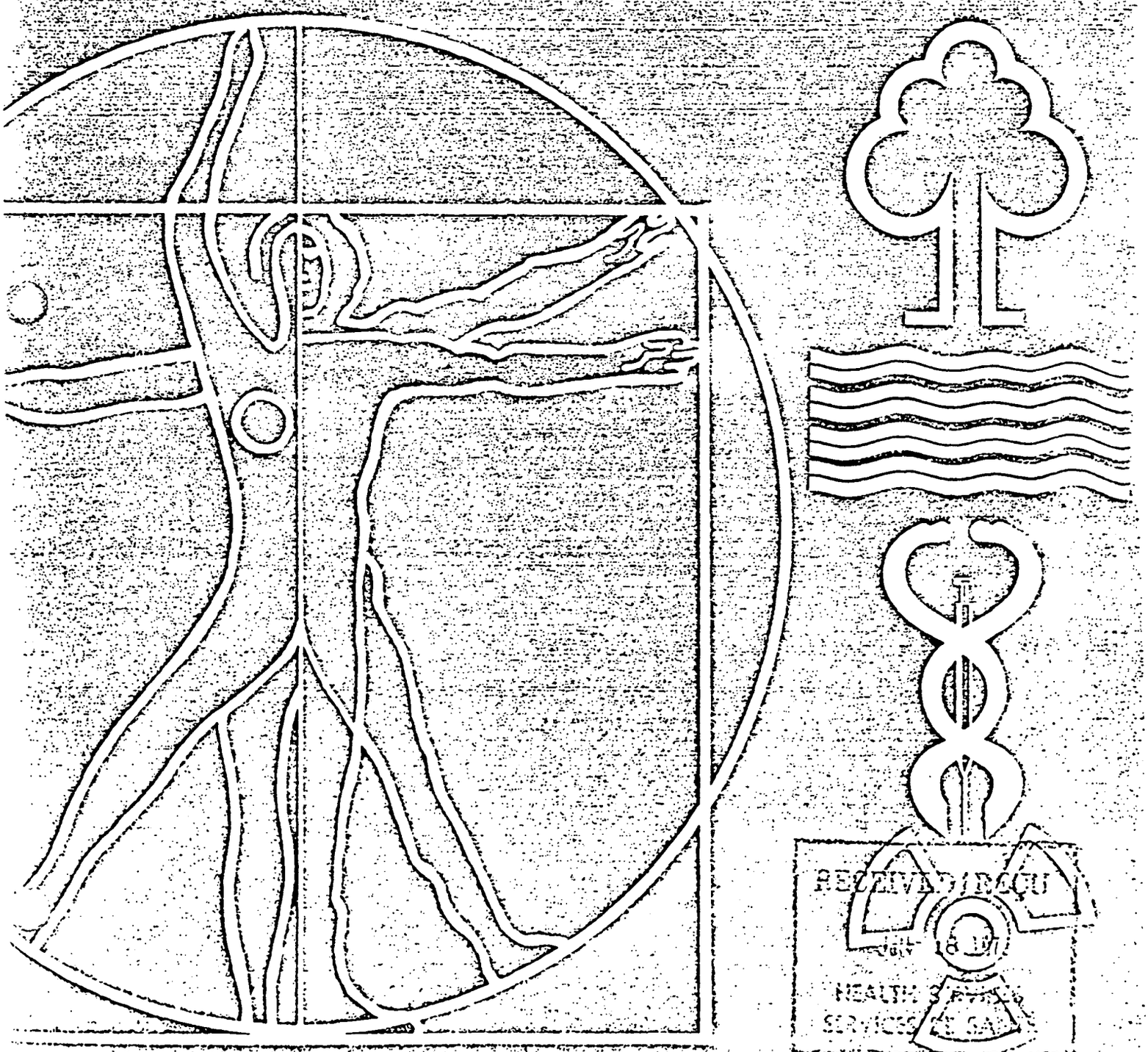
July 23, 1990

APPENDIX 4

78-EHD-21

Health and Welfare Canada
Santé et Bien-être social Canada

methylcyclopentadienyl manganese tricarbonyl (mmt)



METHYLCYCLOPENTADIENYL MANGANESE TRICARBONYL (MMT)

An Assessment of the Human Health Implications of its Use as a Gasoline Additive

Environmental Health Directorate
Health Protection Branch

Published by Authority of the Minister of
National Health and Welfare

78-EHD-21

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FOREWORD

This Report was prepared by staff of the Bureau of Chemical Hazards, Environmental Health Directorate, Health Protection Branch, Department of National Health and Welfare. Available information on Methylcyclopentadienyl Manganese Tricarbonyl (MMT) has been reviewed in order to evaluate possible adverse human health effects resulting from its use as a primary antiknock additive in gasoline. This review has been issued as an Environmental Health Directorate publication in anticipation that such a document will prove useful to other government agencies and private groups concerned with ambient air quality.

Acknowledgement is given to Miss M.E. Meek, the principal author, and to Dr. R. Bogoroch for contributing to the preparation of this Report. The provision of extensive information by the Ethyl Corporation is also greatly appreciated.

SUMMARY

At present, Methylcyclopentadienyl Manganese Tricarbonyl (MMT) is added to fuel oil to suppress smoke formation and to improve combustion; current usage of this additive in gasoline is believed to be quite limited. As the amount of unleaded fuel being produced increases, MMT is one additive being given careful consideration as a primary antiknock compound. This Report deals with the possible health implications of its widespread use in gasoline.

MMT is not manufactured in Canada at present. However, its increased use as a fuel additive could result in exposure of individuals involved in the refining and distribution of gasoline. It has been evaluated as safe for intact or abraded skin contact (NIOSH criteria); the American Conference of Governmental Industrial Hygienists Threshold Limit Valve (TLV) is 0.1 ppm - "skin". The "skin" notation is intended to suggest appropriate measures for the prevention of cutaneous absorption, so that the TLV is not invalidated.

Exposure of the general population to MMT from its use in gasoline would be minimal, since very little (0.1 %) is emitted in the exhaust. The most significant environmental consequence of the use of MMT as a fuel additive is the resulting discharge of manganese to the air, since the principal emission product is Mn_3O_4. Therefore possible health effects of an increase in atmospheric manganese levels are considered. The U.S. E.P.A. estimates that manganese concentrations under worst conditions would increase to less than 5 $\mu g/m^3$ for a 24-hour averaging time. Review of available limited information on industrial and community exposure to manganese and results of studies in animals of chronic inhalation of manganese exhaust products leads to the conclusion that there is no evidence at present to indicate that expected ambient manganese concentrations would constitute a hazard to human health. Data on secondary effects of the use of MMT in gasoline (effects on other emissions and atmospheric reactions) are limited and contradictory; no conclusions can be made at this time about their possible health implications. Recommendations for research to allow a more thorough evaluation of the possible health effects of the use of MMT in gasoline are included.

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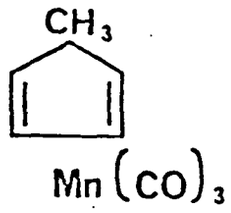
A. IDENTITY, PROPERTIES, AND ANALYSIS

A.1. Physical and Chemical Properties



Methylcyclopentadienyl Manganese Tricarbonyl (MMT) (MCMT)
$C_9H_7O_3Mn$ M.W. 218.1

Alternative Names: Manganese Cyclopentyltricarbonyl (MCPT), Combustion Improver -2 (CI-2), Antiknock -33X (AK-33X)

Appearance: orange liquid; faint, pleasant, herbaceous odor

Freezing Point (°C)	-2.2
Boiling Point (°C)	233
Melting Point (°C)	1.5
Flash Point (COC), (°C)	93.3°
Specific Gravity (H_2O - 1)	1.38

Vapour Pressure (mm Hg)

20 °C	0.051	mm
25 °C	0.1	mm
61 °C	1	mm
100 °C	9.3	mm
160 °C	100	mm
233 °C	760	mm

Solubility (25 °C)

Water	70 ppm
Glycerine	5 %
N-Hexane	Miscible
N-Heptane	Miscible
Isooctane	Miscible
Toluene	Miscible
Ethanol	Miscible

Thermal Stability: decomposes very slowly at 200 °C and fairly rapidly at 300 °C in inert atmosphere; the presence of oxygen increases the rate of decomposition.

MMT in structurally similar to ferrocene, in that the methylcyclopentadiene ligand is π-bound to manganese. MMT is further classified as a penetration complex because dissimilar ligands are bonded to the manganese atom. The pure compound contains 25 % manganese by weight.

A.2. Analytical Methods

Analysis for MMT in gasoline or liquid fuels generally involves an atomic absorption spectrophotometric determination of manganese.(1)

The U.S. National Academy of Sciences has suggested that procedures now being used for the determination of MMT in gasoline or liquid fuels might be modified to be suitable for its analysis in air.(2) At concentrations above 0.1 mg/l, MMT in air has been determined in one study, by passage through fritted disc absorption towers containing glacial acetic acid and subsequent analysis for manganese by the periodate method.(3) At lower concentrations, it has been determined by passage through absorption towers containing ethyl alcohol and analysis for manganese by the formaldoxime method.(3)

B. USE AND PRODUCTION

B.1. Use

Methylcyclopentadienyl manganese tricarbonyl is added to fuel oil to suppress smoke formation and to improve combustion. Typical treatment levels are 0.025 g of manganese per gallon of fuel oil for boilers and 0.08 - 0.5 g per gallon for turbines.

MMT is also used as an antiknock additive in gasoline. At a concentration of 0.125 g of manganese per gallon of gasoline, MMT provides, on the average, about 2 road octane numbers.[4] While originally marketed in the late fifties and early sixties as a secondary antiknock for leaded fuels, it has been marketed since 1974 as a primary antiknock additive for unleaded gasoline which is now required for cars equipped with catalytic converters. Current usage of this additive in gasoline is believed to be quite limited. As the amount of unleaded fuel being produced increases, MMT is one additive being given careful consideration as a primary antiknock compound. The maximum concentration of manganese in gasoline recommended by the Ethyl Corporation is 0.125 g per gallon.*

B.2. Production

MMT has been synthesized by several methods:[5]

1. $(Mn(CO)_5)_2$ + excess $(CH\text{-}C_5H_5)$ $\xrightarrow[100\text{-}300\ ^\circ C]{\text{tetrahydrofuran}}$ $CH_3C_5H_4Mn(CO)_3$

   100 parts 800 parts

2. $MgCl_2 + CH_3C_5H_5 + Fe(CO)_5 + \text{N,N'-dimethylformamide} \rightarrow CH_3C_5H_4Mn(CO)_3$

Reaction 2 is carried out with the use of a Mn electrode, pressured to 1000 psi with CO_2; 25-30V and current density of 0.1 A/cm^2 at 195 °C for 3 hr.

MMT is not manufactured in Canada; it is produced only by Ethyl Corporation at a multi-products facility in Orangeburg, South Carolina. Production of MMT began in the late 1950's, reached and maintained a level of several hundred thousand pounds per year through most of the late 1960's and grew in the last few years to about 1,000,000 pounds per year. Most of the MMT marketed is used at present for smoke control in gas turbine generators.

*All gallons refer to U.S. gallons
1 U.S. Gallon = 3.785 litres = 0.8327 Imperial gallons

B.3. Accidental Spillage and Emergency Procedures

Procedures to be followed in the event of spillage or leakage, as recommended by the manufacturer are as follows:(5)

A spill or leakage of MMT should be reported immediately to Ethyl Corporation, Baton Rouge, Louisiana (Telephone 504-344-7147).

These procedures should also be closely followed:

1. Personnel

In case of contact, personnel should immediately remove all contaminated clothing while flushing the contact areas, e.g., skin and eyes, with plenty of water for at least fifteen minutes. The skin should then be washed thoroughly with soap and water. For eyes, get medical attention. Contaminated clothing should be removed to an isolated location for decontamination or disposal.

2. Clean-up in Open Areas

Maximum ventilation should be provided in the area of the spillage or leakage and personnel should avoid inhalation of MMT vapors. To avoid eye and skin contact, wear chemical splash goggles or face shield, polyethylene, neoprene or vinyl gloves and apron, and boots where necessary. Absorptive material such as rags may be used to assist in the removal of the spill. The contaminated area should then be rinsed with kerosene, diesel or light fuel oil, followed by thorough washing with soap and water. All contaminated materials and rinsings should be removed and transferred to an isolated location for disposal. CAUTION must be exercised in the use of these solvents to avoid a combustion hazard. All sources of ignition must be eliminated from the area until free of combustible vapors.

3. Clean-up in Confined Areas

If the MMT leakage or spillage is in a confined area, efforts should be made to provide adequate ventilation to the area with exhaust fans, etc. In addition, precautions should be taken during clean-up procedures, as described above, to avoid possible inhalation of lingering vapors. A FULL FACE PIECE CANISTER (ORGANIC VAPOR TYPE) MASK should be worn in a ventilated area. If good ventilation cannot be provided, AIR SUPPLIED RESPIRATORY EQUIPMENT must be used during clean-up procedures.

4. Decontamination Procedures - (To be conducted in an isolated area)

   a. Clothing - Contaminated clothing, other than leather goods, may be cleaned for reuse by rinsing in a solvent, such as kerosene, or preferably a non-flammable dry cleaning fluid, followed by thorough washing with soap and water. Shoes or other leather goods cannot be cleaned readily and should be disposed of by burning.

   b. Rags, rinsings, etc. - Contaminated materials should be burned or incinerated.

   c. Soil - For information on the disposal of contaminated soil, phone Ethyl Corp., Baton Rouge, Louisiana, 504-344-7147.

   d. Containers, equipment - All containers and equipment which have been in contact with MMT should be decontaminated in a manner similar to that described for clothing in item 4a. If absorbant material, such as wood, becomes soaked in MMT, it should be removed and burned. Containers must never be reused with any product intended for animal or human consumption.

C. ENVIRONMENTAL INVOLVEMENT

C.1. Emissions of Manganese

The most significant environmental consequence of the use of MMT as a fuel additive is the resulting discharge of manganese to the air. The principal emission product of combustion of methylcyclopentadienyl manganese tricarbonyl is considered to be manganous manganic oxide $Mn^{II}Mn^{III}{}_2O_4$, generally represented as Mn_3O_4. Mn_3O_4 is particulate in nature. Traces of manganic oxide (Mn_2O_3), and the uncombusted compound have also been reported to be present in the exhaust of test vehicles using gasoline with MMT. Typically, only about 0.1 % of the MMT is emitted from the tailpipe unburned; this trace of exhausted compound rapidly decomposes in sunlight to a mixture of manganese oxides and carbonates.(7)

A number of estimates of the increase in ambient levels of manganese expected to result from the extensive use of MMT in gasoline have been made. However, it must be emphasized, that, since current use of MMT is limited, estimates are based on models and these models cannot now be validated for manganese concentrations.

Based on the maximum concentration of manganese initially recommended for use in gasoline (0.125 g Mn/gal), the expected increase in concentration of manganese in the atmosphere has been calculated by the Ethyl Corporation by reference to literature data on lead in air.(7) The levels of lead in air in the U.S. in 1969 varied from 0.00 $\mu g/m^3$ to 4.6 $\mu g/m^3$. At that time, lead was used in gasoline at a concentration of approximately 2.5 g/gallon (20 times the maximum recommended manganese concentration in gasoline). Assuming that manganese and lead emissions to the atmosphere are proportionate, Ethyl has concluded that manganese in air would therefore increase by a maximum of 0.25 $\mu g/m^3$ (1/20 x 4.6) and that 90 % of sampling sites would be expected to have increases of less than 0.1 μg Mn/m^3. The median lead value for all urban sites in 1969 was 1.0 $\mu g/m^3$; therefore the predicted average increase in manganese would be 0.05 $\mu g/m^3$. It must be noted that this model is based on the assumption that the combustion characteristics of an alkyl lead compound (TEL) and an aryl manganese compound (MMT) are similar.

Manganese concentrations resulting from the use of MMT in gasoline have also been estimated by the U.S. Environmental Protection Agency.(8) Estimates were made for various distances from the edge of a 2 -km section of a 6 lane highway based on available roadside measurements for lead and carbon dioxide; a proportionality factor was used for computing manganese concentrations. Based on these estimates it was concluded that the expected manganese concentrations under worst conditions (worst conditions likely to occur

only a few hrs./yr.) would be less than 5 $\mu g/m^3$ for a 24-hour averaging time. It should be noted that the E.P.A. model predicted manganese concentrations 4 to 5 times higher than a similar Ethyl highway model.

A number of other estimates, also based on lead concentrations in ambient air, have appeared in the literature; the increase in atmospheric manganese, if MMT is used in gasoline at a maximum concentration of 0.125 g/gallon, has been estimated by one author to be 0.35 $\mu g/m^3$ with a total yearly average of about 1.2 - 1.5 $\mu g/m^3$.[5] Based on similar assumptions, it has also been stated that if all gasoline in California contained MMT at the maximum recommended concentration (0.0625 g/gal), the annual average contribution to urban airborne manganese concentration would be only 0.07 to 0.14 $\mu g/m^3$.[9] The maximum monthly average manganese concentrations from MMT would be 0.09 to 0.38 $\mu g/m^3$.

C.2. Other Emissions

Besides the increased ambient levels of manganese that will result from the use of MMT in gasoline, a number of other environmental consequences of its use as a primary antiknock in gasoline have been identified:[10]

1. The use of MMT in gasoline appears to result in increased levels of total particulate that cannot be accounted for on the basis of increased manganese emission alone. Manganese also appears to have at least a minor effect on emitted particulate size distribution.
2. The use of manganese in gasoline appears to result in increased aldehyde emissions.
3. The effect of manganese on the emission of polynuclear aromatic hydrocarbons is not yet clear.
4. Manganese results in increased emissions of hydrocarbons; effects on carbon monoxide and nitrogen oxide emissions are less clear.

Available information on these effects is limited and often contradictory; further research is required before any conclusions can be drawn about secondary effects of the extensive use of MMT in gasoline.

C.3. Atmospheric Reactions - Catalysis of the Formation of Sulfur Trioxide from Sulfur Dioxide

Sulfur dioxide is emitted during the combustion of fossil fuels that contain sulfur as an impurity. SO_2 is considered to be a mild respiratory irritant; there is no evidence to suggest that it causes adverse health effects in man at concentrations present in urban air.

However, under conditions of high humidity in the presence of particulate material, sulfur dioxide is converted to sulfuric acid and particulate sulfates, compounds which are more irritating to the respiratory system than SO_2 itself. Manganese is one of the most effective catalysts for SO_2 oxidation.[5, 11, 12] The rate of formation of H_2SO_4 triples when manganese concentrations double and increases linearly with an increase in SO_2 concentration.[5]

There is conflicting evidence in the literature about the efficiency, at various concentrations, of manganese as a catalyst for SO_2 oxidation. Estimates of the rate of atmospheric catalytic oxidation of SO_2 under similar environmental conditions and with similar concentrations of manganese vary considerably.[11-14]

There is little information available on the efficiency of manganese as a catalyst for SO_2 oxidation at the ambient concentrations that are expected from the use of MMT in gasoline. To verify extrapolations from data in the literature on the effect of low levels of manganese in air on SO_2 oxidation, the Ethyl Corporation has conducted studies in a 3,500-ft^3 black polyethylene bag with a controlled atmosphere containing SO_2, water vapor, ammonia and exhausted manganese.[7] In the absence of ammonia, the SO_2 reaction rate was unchanged with manganese concentrations of 4 $\mu g/m^3$. At very high concentrations of manganese (36 $\mu g/m^3$), no effect occurred below 70 % relative humidity and the oxidation rate increased rapidly only when the relative humidity was above 90 %. The addition of ammonia to the bag at 20 $\mu g/m^3$ more than doubled the rate of SO_2 conversion to SO_3. These results suggest that the normal amount of ammonia in the air is probably the rate-controlling factor in atmospheric SO_2 oxidation and that the general use of MMT in gasoline would have little effect on the rate of SO_2 oxidation in the atmosphere. However, further data is required to validate these results.

The Calspan Corporation, under contract to E.P.A., has determined that, at manganese concentrations of approximately 0.5 $\mu g/m^3$, the presence of manganese had a measurable impact on visibility in a 20,000 cu ft chamber after 23 hours irradiation.[15] However, this decrease in visibility cannot be attributed solely to the presence of aerosol sulfates.

D. OCCURRENCE, RESIDUES, AND CONTAMINATION - MANGANESE

Since the principal exhaust product of MMT is Mn_3O_4, this section will summarize concentrations of manganese in the environment to place in perspective levels that can be expected from the extensive use of MMT in gasoline.

D.1. Soil, Air, Water and Food

Manganese does not occur naturally as a metal but is present in over 100 common salts and minerals widely distributed in rocks, soils and on the floors of lakes and oceans. It is most often present in the form of manganese dioxide, manganese carbonate and manganese silicate. It is invariably present in arable soil and is associated in trace quantities with every kind of plant and animal tissue.(16) The average manganese content of Canadian soil is 800 ppm.(17) Soil concentrations of manganese range from 0 to 7000 ppm.(11)

Manganese is generally present in natural surface waters in dissolved and suspended forms in concentrations less than 0.05 mg/l. Data from Canadian national surface water stations indicate that only 3 areas recorded levels above 0.05 mg/l during the years 1974-1976.(18) Higher levels of manganese in freely flowing river water are most often associated with industrial pollution. Higher levels are also found under reducing conditions such as exist underground or may occur in some lakes or reservoirs.

For sixty-seven percent of 84 national sampling sites for drinking water, manganese levels lie in the range of less than 0.01 mg/l to 0.02 mg/l. Levels in excess of the present Canadian limit in drinking water of 0.05 mg/l were recorded at 25 percent of the 84 national stations sampled.(18)

Manganese in the atmosphere is generated industrially, being emitted from various sources primarily as manganese oxides. The total estimated atmospheric emission of manganese in Canada in 1972 was 6625 tons; 99.4 % resulted from ferroalloy and steel production. Burning of coal for generation of electricity, burning of solid waste and sewage sludge in municipal incinerators and application of manganese containing fungicides constituted other significant sources of manganese emissions in Canada in 1972.(19) The use of light and heavy oils in stationary sources was not a significant source of manganese emissions.

Analysis of air samples collected in the Montreal area in 1967-1968 shows values of approximately 0.03 $\mu g/m^3$ for manganese content.[20] Slightly higher levels for the manganese content of air samples collected in various locations in Toronto have been reported. The manganese content of air samples in the vicinity of urban metal refineries averaged 0.062 $\mu g/m^3$ (0.018 - 0.178). Manganese levels in samples from other areas in Toronto averaged 0.069 $\mu g/m^3$ (0.038 - 0.166).[21] These average values fall well within the range of manganese concentrations in air of areas, both rural and urban, considered by the U.S. Environmental Protection Agency not to be polluted by significant amounts of manganese emission.[8] In the U.S., manganese concentrations in urban air average 0.10 $\mu g/m^3$ and range as high as 10 $\mu g/m^3$.[22]

The manganese content of foodstuffs varies considerably. Generally, low concentrations are found in dairy (average 0.12 $\mu g/g$) and meat groups (average 0.33 $\mu g/g$). Manganese is relatively evenly distributed throughout all the food groups derived from plant sources (average 2.66 $\mu g/g$).[23]

It has been estimated that the average daily intake of manganese for Canadians is 2 μg through inhalation, 3600 μg in food and 40 μg in water.[24]

E. EXPERIMENTAL TOXICOLOGY - MMT

The reported low emission rate and instability of MMT in the atmosphere suggest that exposure of the general population to the parent manganese compound in exhaust would be minimal. Sections E and F have been included to provide information about possible health implications for individuals engaged in the manufacture, distribution, blending, testing and use of MMT.

E.1. Metabolism

When methylcyclopentadienyl^{54} manganese tricarbonyl was administered orally and intravenously to rats, most of the labelled manganese was rapidly excreted in the urine and feces.(25) Seventy-three percent of an oral dose of 2.5 mg MMT (0.625 g Mn) was excreted within 24 hours; 36 % of this amount was present in the urine. Such a high percentage in the urine is not typical of normal manganese excretion. Analysis of the urine and feces indicated that the MMT was metabolized and that the manganese was excreted in an inorganic form.

The liver, kidney and lungs contained the highest concentrations of manganese after MMT administration. The tissue distribution after a single oral dose was similar to that for manganese, except for the high concentration found in the lungs and abdominal fat.

In rabbits and rats exposed to MMT in dermal irritancy tests, most of the MMT absorbed into the system was rapidly excreted.(26)

E.2. Acute Toxicity

MMT can be absorbed from the enteric tract, through the skin or through the lungs in sufficient amounts to cause serious illness and death in experimental animals. LD_{50} values vary widely, depending upon the species, the route of administration and the diluent.(27) There is also a wide variation in mortality response to a specific dosage of MMT; however, exceptional range in individual susceptibility is not peculiar to this manganese compound but is characteristic of manganese toxicity in general.

The signs of illness resulting from the administration of lethal doses of MMT are similar in all species regardless of the route of absorption and consist of initial mild excitement and hyperactivity, tremors, severe tonic spasms, weakness, slow and labored respiration, occasional mild clonic convulsions and terminal coma. Animals given sublethal amounts exhibit similar but less severe manifestations and, after suffering temporary losses in weight, appear to recover completely in 2 to 6 weeks. Residual neurologic effects have

not been noted. The predominant pathologic changes are found in the kidneys and livers of experimental animals.[27] In animals dying from exposure to MMT, concentrations of manganese are elevated in selected tissues.[28]

It should be noted that toxic effects of exposure to MMT are not the result of acute manganese toxicity since manganese toxicity occurs at much higher dosage levels and the pattern of hepatic lesions is markedly different from that seen in acute manganese toxicity.

(i) Oral

Oral LD_{50} values for several species are summarized in Table 1.[27] Hysell et al (1974) reported the LD_{50} of MMT administered orally to rats in Wesson oil to be 58 mg/kg,[28] which is well within the range of values reported in Table 1.[27]

Table 1 - The Immediate Oral Toxicity of Methylcyclopentadienyl Manganese Tricarbonyl (from Ref. 27)

Species	Preparation Administered	LD_{50} as MMT mg/kg (95 % C.L.)	
		Male	Female
Guinea Pig	Undiluted	-	905 (500 - 1640)
Mouse	2 g/100 ml peanut oil	352 (222 - 558)	
Rabbit	10 g/100 ml peanut oil	-	95 (72 - 124)
Rat	Undiluted	70	8
Rat	2 g/100 ml peanut oil	176 (160 - 194)	96 (70 - 130)
Rat	2 g/100 ml peanut oil	38 (33 - 34)	23 (21 - 25)
Rat	5 g/100 ml peanut oil	24	24
Rat	10 g/100 ml peanut oil	33	35
Rat	5 g/100 ml kerosene	40	47
Rat	10 g/100 ml kerosene	40	80
Rat	10 g/100 ml kerosene	18 (11 - 24)	9 (6 - 12)
Rat	10 g/100 ml kerosene	24 (23 - 25)	17 (15 - 18)

(ii) Dermal

When MMT was diluted with peanut oil (10 g/100 ml) and kept in contact with the intact skin of rats for 6 hours, the calculated LD_{50} was 665 mg/kg.[27]

On the basis of direct dermal irritancy and cellular toxicity tests in rabbits, MMT has been evaluated as safe for intact or abraded skin contact (irritancy grade of 1 on a scale of 4, NIOSH criteria).[29]

Various concentrations of MMT in gasoline (0.4 g/l, 2.4 g/l, 16 g/l) were applied for extended periods of time on the skin of rabbits and rats. No significant adverse effects attributable to MMT were observed in rats. At the higher concentrations, vacuolar degeneration of the liver and kidney was noted in some of the rabbits. The severity of these effects was greater in the group given the higher dose.[26]

(iii) Inhalation

The one hour LC_{50} for rats by inhalation has been reported to be 220 mg/m^3.[27]

E.3. Chronic Toxicity and Clinical Effects

Inhalation

In one study, young mature dogs, cats, rabbits, guinea pigs, mice and rats were exposed repeatedly (7 hours per day, 5 days per week for up to 30 weeks) to various concentrations of MMT in air.[3] Exposure to levels of 14 - 17 mg/m^3 produced mortality only in rats and mice but not in other species. All animals survived 150 daily exposures to 6.4 mg/m^3 without significant effect or pathological change. Pathological changes resulting from the higher concentrations were observed primarily in the liver and kidneys. Two female beagle dogs survived 100 daily exposures to 12 mg/m^3 without exhibiting any signs of illness or pathologic abnormalities. In general, animals dying during chronic inhalation exposure exhibited chronic bronchitis and peribronchitis. Interpretation of results in this experiment was complicated by the occurrence in some animals of occasional diseases presumably unrelated to the experimental procedure.

A number of additional studies to determine toxicological effects on experimental animals of inhalation of MMT vapour have been initiated.[30, 31]

F. HUMAN HEALTH EFFECTS - MMT

F.1. Acute Toxicity

Improper handling of MMT resulted in contact on the hands and forearms of 6 individuals for 5 to 30 minutes. Exposure produced a variety of symptoms including metallic taste, headache, nausea and dyspnea; these symptoms disappeared within 2 hours. Two cases of more severe exposure (1 1/2 hours) resulted in high manganese (46 - 137 µg Mn/l) content of urine soon after exposure. Within 2 weeks, urine Mn was within the normal range of 2 - 3 µg/liter. None of the exposed men had significant symptomatology either initially or later. No change in physical or neurological examination was noted in any of the cases.[32]

F.2. Chronic Toxicity and Clinical Effects

In 1971, the American Conference of Governmental Industrial Hygienists first established the present Threshold Limit Value for MMT of 0.1 ppm (0.22 mg Mn/m^3).[33] Threshold Limit Values refer to airborne concentrations of substances and represent conditions under which it is believed that nearly all workers may be repeatedly exposed day after day (8-hour workday) without adverse effect. The TLV for MMT carries a "skin" notation which is intended to suggest appropriate measures for the prevention of cutaneous absorption so that the threshold limit is not invalidated.

G. PUBLIC HEALTH EFFECTS

Exposure of the general population to MMT from its use in gasoline would be minimal, since very little (0.1 %) is emitted in the exhaust. Since the most significant environmental consequence of the use of MMT as a fuel additive is the resulting discharge of manganese to the air, this section deals mainly with possible health effects of an increase in atmospheric manganese levels.

G.1. Emissions of Manganese

(i) Manganese-Essentiality and Biological Role

Manganese is an essential element in animals and man. It is required as a cofactor in a number of enzymes; it is essential to arginase and alkaline phosphatase in the liver; it plays a role in the proper functioning of flavoproteins and in the synthesis of sulfated mucopolysaccharides, cholesterol, and hemoglobin; and it is implicated in carbohydrate metabolism, lipid metabolism, oxidative phosphorylation, growth, reproduction, and brain function.[2] Recently its presence in drinking water has been inversely associated with cardiovascular mortality.[34]

In animals, experimentally induced or naturally occurring manganese deficiency has resulted in the following: lack of growth, abnormalities of bone (deformities, dislocations, and perosis) and of reproductive function (ovarian dysfunction, testicular degeneration, poor lactation, frequent abortions, and high mortality among the young) and symptoms of central nervous system disturbance (lameness and stiffness of legs, ataxia, loss of equilibrium).[35] Although no specific syndrome in man due to manganese deficiency has been described, it has been suggested that there may be an association between manganese deficiency and a number of disorders such as anemia, bone changes in children, and lupus erythematosus.

Minimal human nutritional requirements for manganese have not been established. However, based on the fact that no manganese deficiency in humans has yet been documented and that the normal daily manganese intake ranges from 2 to 7 mg per day,[36] it is reasoned that the minimum daily requirement is probably less than 2 mg per day. It has been determined that a daily intake of 3 to 7 mg per day will give a body burden of 12 to 20 mg in a 70 kg man.[2, 37]

(ii) Manganese - Metabolism

The main routes of absorption of manganese are the respiratory and gastrointestinal tracts; negligible absorption of inorganic manganese occurs through the skin.[38] Organically-bound manganese may be absorbed by the cutaneous route.[2]

There seem to be efficient homeostatic mechanisms which keep manganese concentrations in the body and in tissue relatively constant despite variations in the diet.[9] Manganese in the body is regulated primarily by excretion rather than by both absorption and excretion. The primary mode of manganese excretion is via the gastrointestinal tract. After absorption, manganese accumulates in the liver from where it is rapidly excreted in the bile for eventual elimination in the feces. Some of the metal is excreted through the pancreatic secretions and some directly through the wall of the gut. Very little (0.1 - 2 %) is eliminated in the urine. In normal individuals the daily urinary excretion rate is 1 - 8 µg/l;[39] variations in dietary manganese have little effect on the urinary manganese excretion. However, Horiuchi and co-workers noted a parallel between the concentration of manganese in air and proportionately elevated levels of manganese in whole blood and urine of industrial workers.[40] Significant correlation also was observed between manganese content of urine and neurological findings in workers in whom manganese intoxication was recent. The excretion of manganese appears to occur in two stages: 30 % is eliminated with a halftime of 4 hours, the remainder with a halftime of 39 days.[2]

The biological half-life of manganese in man is influenced by a number of factors including the intake of manganese, the state of iron storage and the hemoglobin concentration. The presence or absence of other cations can also modify manganese excretion. For example, oral and intraperitoneal tracer studies have shown that, in weanling rats fed a low calcium diet, the excretion of manganese increased.[41]

The bones contain the highest concentration of manganese, about 25 % of the total body manganese.[42] Cotzias postulated that "each animal tissue contains a concentration of manganese which is almost characteristic of the individual organ and independent of the species of the animal with which the tissue has originated".[43] Generally, organs and tissues do not accumulate large concentrations of manganese.[2, 8] However, wide variations of manganese concentration have been reported in the literature, especially for blood levels.[2, 42] The normal blood manganese concentration is generally accepted as 20 - 100 µg/l.

According to Schroeder, manganese in man neither accumulates nor declines with age; it passes the placental barrier, is stored in the newborn and is present in milk.[44] Dobrymina and Davidjan on the other hand, report that most organs other than the liver show a decrease in manganese content with age.[68]

Manganese accumulates in pigmented areas of the body (retina, dark hair, and skin) presumably through its little understood role in the metabolism of melanin and its precursors.[2] Although the manganese content of scalp hair may not correlate with environmental levels,[45] elevated levels in chest hair may be of diagnostic significance.

It has been reported that in experimental animals, manganese accumulates to a greater extent in organs after inhalation than after ingestion, the principal sites of accumulation being the lungs, the small intestine, the liver, the kidneys, pancreas, brain, and muscle tissue.[46] However, this statement seems to be an over-simplified summary of studies in which mice inhaled manganese dioxide dust in concentrations averaging 8,910 $\mu g/m^3$ every 2 hours for eight days (particle size less than 3 microns).[9] Concentrations in most tissues or organs were increased in the inhalation series, compared to controls with similar oral intake of manganese. The major differences in tissue levels, which could possibly be due to local deposition, were found in the lungs and trachea. High concentrations possibly attributable to swallowing of particles, were also found in the stomach and small intestine.

(iii) Manganese Toxicity

Manganese is regarded as one of the least toxic elements. Chronic ingestion experiments in rabbits, pigs, and cattle at 1000 - 2000 ppm dose levels have shown no effects other than a change in appetite and reduction in metabolism of iron to form hemoglobin.[2] The toxicity of manganese varies with the valence state, with the route of administration and, when inhaled, with particle size. To date there is no evidence of sex difference in susceptibility to inorganic manganese intoxication.

(a) Industrial Exposure

Inhalation appears to be the main route of absorption in cases of intoxication in man. According to Mena, who used radio-tracer methods, 60 to 70 % of inhaled manganese dust is swallowed and absorbed through the gut while the remaining particles of diameter size less than a few tenths of a micron diffuse across lung alveolar membranes and eventually enter into the systemic

circulation.[37] Cooper has stated that although definitive studies are not available, it is probably safe to assume absorption of 50 % or less for particles in the respirable range, i.e., below 3 micrometers in diameter.[9]

Toxicity in man is usually the result of chronic inhalation of high concentrations of manganese dusts from industrial sources.[39, 47-52] In these cases, there is apparently no correlation between age, duration of exposure and onset of symptoms; symptoms differ considerably from case to case. Onset may occur as little as three months or as long as 20 years after exposure. The severity of the symptoms, however, often is proportional to the length and intensity of exposure. The principal effects of long-term occupational exposure to inorganic manganese compounds are the production of "manganese pneumonia" or pneumonitis[38] and more commonly, manganism.

Clinical signs of manganese pneumonitis are initially those of acute alveolar inflammation. Breathing is markedly labored and difficult, respiration shallow and gasping. Cough and expectoration are rare. The illness changes, however, after the third day from frank pneumonia to less well defined localization and discrete pleural involvement. Fatality can ensue from heart failure between the fifth and tenth day.[5]

The early symptoms of manganism include psychosis resembling schizophrenia. The onset of psychiatric symptoms is usually insidious and progressive. The first manifestations are subjective complaints of asthenia, anorexia, apathy, insomnia or somnolescence and a decrease in the rate of performance of motor acts. These are followed by overt behavioural changes. The correlation between symptoms and histological pathology at this stage is obscure. Later symptoms reflect extrapyramidal disorders similar to Parkinson's disease, the neurological manifestations and biochemical alterations of which have been detailed by Cotzias et al.[49, 53] Removal from exposure in the initial stages results in remission of symptoms. However, neurological damage is not reversible.

The lowest daily and total exposure level to manganese which will result in symptoms of toxicity in man has rarely been systematically determined. From a review of available literature on industrial manganese intoxication, it has been concluded that verified cases of neurological disorders have been observed in man after prolonged occupational inhalation of dusts containing over 5000 $\mu g/m^3$.[9] Acute pulmonary disease has occurred in the same

dosage range. Another author has reported that manganese ore miners in Chile, Brazil, Morocco and South Africa, manganese steelworkers in Pennsylvania and manganese dry battery workers in Eqypt and Great Britain have shown incidence of neurological disorders and respiratory disease at concentrations ranging from 5,000 $\mu g/m^3$ - 60,000 $\mu g/m^3$.[5] The Threshold Limit Value for manganese and compounds (the airborne concentration to which it is believed that nearly all workers may be repeatedly exposed without adverse effect) is 5 mg/m^3 (5,000 $\mu g/m^3$).[33]

(b) Community Exposure

There have been some reports in the literature on the influence of manganese emissions on inhabitants living in the vicinity of manganese industries. However, reliable data on concentrations of manganese present in the air of these communities is lacking and it is difficult, therefore, to draw conclusions about levels of manganese that have caused symptoms of manganese toxicity in the general population.

Increased incidence since 1939 of lobar pneumonia in Sauda, Norway, has been attributed to emissions of manganese from a ferromanganese smelting plant.[54, 57] Post mortem examination of individuals who had died of lobar pneumonia in Sauda indicated that the manganese concentration in lung tissues was considerably higher than normal. As well, the rise in morbidity and mortality caused by lobar pneumonia paralleled the increase in the amount of ferromanganese discharged by the plant. The concentration of manganese in the atmosphere was reported to be a maximum of 64 μg Mn_3O_4 (46 μg Mn/m^3) at a point 3 km from the plant. However, the method used to analyze for manganese was found to give low results and the total intake of manganese through inhalation is not known. Emissions from the plant also included other toxic compounds (dry matter in the smoke contained 54 % silica and 2.56 % manganese oxide near the plant).[2]

A similar situation in the vicinity of another ferromanganese plant in Aosta, Italy, in 1947, has been reported.[58] However, no quantitative data on the levels of airborne manganese present were included. The author of the report was also somewhat hesitant to attribute the increased pneumonia incidence in Aosta to manganese, in view of the fact that morbidity incidence decreased even though ferromanganese production continued.[9]

There have been a number of more recent reports from Japan relating pulmonary symptoms in children to increased manganese levels resulting from emissions from a ferromanganese plant.[59, 60] However, the analytical data included in these studies are insufficient to determine critical exposure levels; most data were reported in terms of dustfall. Manganese dustfall measured monthly for 3 years averaged about 200 kg/km^2 per month in the vicinity of the plant, compared with 8 kg elsewhere in Kanazawa. Some 24 hour suspended particulate measurements made in the plant neighbourhood to 300 meters ranged from 4 to 260 µg Mn/m^3. A comparative study of two groups of middle school students, investigating subjective symptoms, medical history, present condition and pulmonary function test by respirometer, indicated that students in a school 100 m away from the plant had a higher incidence of nose and throat symptoms, a higher history of pneumonia and lower pulmonary function than did students in a similar school remote from the manganese plant. A resurvey after controls were installed in the ferromanganese plant (manganese dustfall was reduced from 200 kg/km^2 to 20 kg/km^2) showed that the health effects identified were mainly reversible; the prevalence of nose and throat symptoms in the polluted school decreased to a level comparable to that of the control school.

(c) Animal Models - Exposure to Manganese Aerosols

There are few reliable data on levels of manganese in air that have caused symptoms in man in community and industrial situations. However, several animal studies have been conducted to evaluate possible toxicity resulting from chronic exposure to manganese aerosols at concentrations approaching ambient levels expected from the use of MMT in gasoline as a primary antiknock agent.

The primary exhaust product of combustion of MMT, Mn_3O_4, in much less toxic than is MMT. Consumption by rats of from 4 - 8900 mg/kg body weight of Mn_3O_4 caused no mortality or apparent tissue damage.[61] Even daily oral doses 150 times greater than the oral LD_{50} of MMT to rats were only slightly toxic.

In rats and hamsters exposed for 56 consecutive days to irradiated and nonirradiated automotive emissions containing increased concentrations of manganese particulate (average, 117 µg/m^3) resulting from the addition of MMT, no gross changes in general condition or appearance of the animals

were observed.[62] Microscopic examination of tissue revealed no changes which could be solely attributed to the presence of manganese or MMT. Nevertheless, manganese concentrations in several tissues from exposed animals were elevated significantly; the concentration of manganese in the brain tissue, liver and lungs of the exposed animals was on the average 1.8, 1.69 and 1.5 times the concentration in the respective tissues of the control animals.

In monkeys and rats exposed continuously for 9 months to a manganese oxide aerosol produced by combusting vapours of MMT (11.6, 112.5, 1152 $\mu g/m^3$ Mn), no apparent adverse effects were observed.[63] Body weights were not adversely affected by the exposure conditions; EMG and limb tremor evaluations were totally negative with respect to effects due to exposure conditions. Hematologic evaluations indicated an increase in hemoglobin and mean corpuscular hemoglobin concentration in the high level groups of both rats and monkeys as compared to the control group. However, the difference was small and the values remained within an acceptable normal range. There were no adverse effects in any of the serum biochemical parameters of either rats or monkeys. Tests of pulmonary function in monkeys were negative as regards adverse effects related to the exposure conditions. Tissue levels of manganese 6 months post-exposure were comparable for all groups in both monkeys and rats. There was some suggestion of slightly elevated lung weights for rats in the high level groups; however, this was probably related to higher body weights. Histopathological evaluations of either monkeys or rats failed to demonstrate any adverse effects which could be related to exposure conditions.

No toxic effects were observed in another study in which rhesus monkeys were exposed continuously for periods of up to 66 weeks to manganese oxide particulates (100 $\mu g/m^3$ Mn) generated through combustion of vaporized MMT.[64] There was small but statistically significant increases in manganese levels in the lungs, livers, pancreas, kidney and heart muscle. Also, concentrations were greater in the brain pallium, basal ganglia, cerebellum and pons. The data yielded no evidence of any alteration in the rate of fecal excretion of manganese induced by respiratory exposure to manganese oxide nor was there any change in the blood manganese levels elicited by exposure.

(iv) Manganese - Acceptable Daily Intake

According to Schroeder, no adverse health effects in humans have been noted with daily manganese intake levels as follows:(44)

	Average (mg)	Range (mg)
Food	3.000	2.0 - 7.0
Water	0.005	0.0 - 1.0
Air	0.002	0.0 - 0.029

G.2. Other Emissions and Atmospheric Reaction Products

Since available information on the effects on other emissions and atmospheric reactions resulting from the use of MMT in fuel is limited and contradictory, no conclusion can be drawn about possible health implications of secondary effects of the use in gasoline of MMT as a primary antiknock additive.

II EVALUATION AND ASSESSMENT

A. RECOMMENDED EXPOSURE LIMITATIONS - MANGANESE

The Threshold Limit Value for manganese and compounds, established by the American Conference of Governmental Industrial Hygienists, is 5 mg/m^3 (5000 µg/m^3).[33] Threshold Limit Values refer to airborne concentrations of substances and represent conditions under which it is believed that nearly all workers may be repeatedly exposed day after day without adverse effects. It is generally accepted that the TLV for manganese and compounds carries a low margin of safety for those occupationally exposed. Limits adopted in some other countries are lower (0.3 - 5 mg/m^3). To date, there are no ambient air quality or stationary or mobile source emission standards for manganese.

B. EXPOSURE LEVELS - MANGANESE

Levels of manganese in the air of Canadian urban communities currently average less than 0.10 $\mu g/m^3$.[20, 21] The U.S. E.P.A. estimates that manganese concentrations resulting from the use of MMT in gasoline under worst conditions would be less than 5 $\mu g/m^3$ for a 24-hour averaging time.[8] Other authors give lower estimates; predicted average annual increases range from 0.05 - 0.35 $\mu g/m^3$.[5, 7, 9]

The average daily intake of manganese in air is, at present, considered to be 2 µg. If MMT is used in the future as a primary fuel additive, daily intake of manganese from air would certainly not exceed and probably would be considerably less than 100 µg, assuming the daily intake of air to be 20 m^3.

Manganese intake is much greater from food than from inhalation or from ingestion of water. The daily dietary intake of manganese in typical Canadian diets has been estimated to be 4100 µg in the Ottawa-Hull area,[65] 3700 µg in Vancouver and 3000 µg in Halifax.[23] The average of these values, 3600 µg, compares with the total dietary intake of manganese in food for the non-occupationally exposed individual in a non-polluted area estimated by Schroeder et al.[44] Generally, only 3-4 % of orally administered manganese is absorbed from the G.I. tract of healthy normal individuals.[37, 67]

Assuming daily water consumption to be 2 litres and the average manganese content of Canadian drinking water to be 20 µg/l, the average daily intake of manganese would approximate 40 µg. There is considerable variation in such estimates, however. Craun and McCabe estimated the average daily intake of manganese from drinking water in the U.S. to be 44 µg.[66] The U.S. E.P.A., on the other hand, considered this value to be 5 µg.[8]

C. ASSESSMENT OF RISK

C.1. Occupational Exposure

Although MMT is not manufactured in Canada at present, its increased use as a fuel additive could result in exposure of individuals involved in the refining and distribution of gasoline. On the basis of NIOSH criteria, MMT has been evaluated as safe for intact or abraded skin contact.[29] The TLV recommended by the ACGIH is 0.1 ppm (0.22 mg Mn/m^3) - "skin".

C.2. Public Health Effects

Based on the limited data available at present, there is no evidence to indicate that ambient manganese concentrations resulting from the use of methylcyclopentadienyl manganese tricarbonyl as a primary antiknock agent in gasoline (maximum 5 $\mu g/m^3$ under worst conditions), would constitute a hazard to human health. Data available on other environmental effects such as catalysis of the formation of sulfur trioxide and effects on other emissions are limited and contradictory; no conclusions can be drawn about the possible health implications of such effects.

The paucity of available toxicological data does not permit the establishment of dose-response relationships for long-term inhalation of manganese in different animal species and man. It has been suggested that verified cases of neurological disorders and pulmonary disease in man have been observed after prolonged occupational inhalation of dusts containing over 5000 $\mu g/m^3$ of manganese.[5, 9] There have also been reports in the literature on the increased incidence of pneumonia and pulmonary symptoms in communities in the vicinity of manganese industries; however, the lack of reliable analytical data on levels of manganese present and the presence of other toxic compounds in the emissions preclude the estimation of manganese concentrations that have caused morbidity in the general population. It appears though, that the levels of manganese in the air of such communities were considerably greater than those expected from the widespread use of MMT in gasoline in non-industrial communities. However, it should be noted that there may be differences in the chemical form, particle size and solubility of manganese in industrial as compared to exhaust emissions.

There are no data available on the effects of chronic exposure to low concentrations of manganese on special groups such as pregnant woman, infants and those with minor respiratory ailments.

Because of the lack of relevant human data on the toxicity of manganese, several preliminary studies on the effects of manganese exhaust products following chronic inhalation exposure using animal models have been conducted. To date, there have been no apparent adverse effects observed in rodents and primates exposed for periods of up to 66 weeks to 11.6 - 1152 $\mu g/m^3$ of managanese, generated by combustion of MMT. Maximum concentrations of manganese expected under worst conditons from the use of MMT as a primary antiknock agent (5 $\mu g/m^3$) fall well below the lower limit of this range of concentrations.

D. RESEARCH NEEDS

Research in the following areas to allow a more thorough evaluation of the health implications of the use of MMT as a primary antiknock agent in gasoline is warranted:

1. Experimentation with test vehicles under controlled conditions to:

   (a) determine maximum levels of manganese in air that can be expected from the use of MMT in gasoline;

   (b) characterize more fully the physical and chemical properties of resulting manganese emissions;

   (c) determine effects of the combustion of MMT in gasoline on emissions such as aldehydes, polynuclear aromatic hydrocarbons, carbon monoxide and nitrogen oxides;

   (d) determine the catalytic efficiency of manganese emissions in the conversion of SO_2 to sulfuric acid and particulate sulfates.

2. Further toxicological data is required to:

   (a) increase present knowledge of the absorption, transport, metabolism, localization and excretion of various manganese compounds in humans;

   (b) determine effects of inhalation of manganese on special risk groups such as pregnant women, infants and those with chronic respiratory diseases;

   (c) establish dose-response relationships for toxicological effects on animals of emissions of manganese from the combustion of MMT.

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APPENDIX 5

THE ROYAL SOCIETY
OF CANADA

LEAD IN GASOLINE

ALTERNATIVES TO LEAD IN GASOLINE

S U P P L E M E N T A R Y R E P O R T

(1) COMMISSION'S CONCLUSIONS

(2) TECHNICAL APPRAISAL BY

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THE COMMISSION ON LEAD IN THE ENVIRONMENT

FEBRUARY 1986

CONTENTS

TERMS OF REFERENCE

COMMISSION ON LEAD IN THE ENVIRONMENT

Purpose

To provide the Minister of the Environment with independent advice on the present and future risks and areas of concern resulting from the presence of lead in the Canadian environment, and

To consider and propose, as may be required, corrective measures to reduce the environmental and health risks associated with lead which may be adopted either independently by the Minister of the Environment or in cooperation with others. The effects of lead in the workplace are specifically excluded from these terms of reference.

Considerations

To fulfil these objectives the Commission is to report on the following:

1. (a) the sources of lead releases in Canada and their relative contributions;

   (b) the pathways by which lead enters the Canadian environment and the means and media by which lead is transported within the environment and to humans;

   (c) the toxicity of lead;

   (d) the potential or actual exposure of, and risks to human and environmental targets in Canada;

2. (a) practical corrective measures, as may be required, to reduce the risks associated with lead based on the Commission's review and assessment of the impact and implications of lead for the environment and for humans;

   (b) the economic, technical, social (where appropriate) and labour implications of reductions in lead releases and exposure from all sources including the implications of eliminating lead in gasoline.

Duration and Reporting

The Commission will sit for three years and provide a progress report by September 1, 1985 on the direction and findings of its review, and a final report including its recommendations by September 1, 1986. The Commission shall continue to sit for a third year to receive and review comments on its reports and to make recommendations on those comments.

The Commission's progress and final reports will be made available to the public.

All written submissions made to the Commission except those deemed by the submittor to contain confidential business information will be made available to the public.

PREFACE

In September, 1985, the Commission reported to the Minister of the Environment on lead in gasoline. Recommendation 12 of that report said that the environmental and health implications of the different octane sources (other than lead) needed to be explored further. This supplementary report presents such a study, and also looks at alternative fuels that may partially replace gasoline in Canadian use.

The Commission decided to proceed as follows:

(i) to ask the Chief Scientist, Dr. M.C.B. Hotz, to prepare a technical appraisal of the actual and potential problems; and

(ii) to present its own conclusions, based largely on Dr. Hotz' overview, on the use of these additives and alternatives in producing unleaded gasoline of suitable octane rating.

These materials are presented in reverse order, so that the reader can get a quick overview of the Commission's opinions. Among these is that little attention has been given to the question. A large volume of reports deals with the health hazards of leaded gasoline. Much less is known about the consequences of removing lead.

The Commission appreciates the help received from National Health and Welfare Canada, the United States Environmental Protection Agency (US EPA) and the Petroleum Association for Conservation of the Canadian Environment (PACE).

F. Kenneth Hare
CHAIRMAN

THE COMMISSION'S CONCLUSIONS

1. The Commission finds that there are many potential alternatives to tetraethyl lead as octane enhancers. Some, however, may have adverse health effects. The pace of conversion should be deliberate enough to allow choice of methods that will ensure that the penalties paid do not exceed the expected health gains, by releasing other toxic substances into the environment. [see Technical Appraisal (TA) pp.1-5]

2. For example, as tetraethyl lead is replaced as an octane source in gasoline by more severe reforming and isomerization, higher concentrations of aromatic hydrocarbons will arise. Such compounds will be present whatever other additives are used, and may themselves be used as additives. Most of the automotive emissions of these compounds will be toluene and xylenes, which are rapidly metabolized and excreted from the human body. Benzene will also be present, however. This aromatic is a potent carcinogen as well as an excellent octane enhancer. [(TA), pp. 11-14].

3. Market trends brought about by the rapid phasedown of lead in the United States have already made the aromatics more valuable as octane enhancers. We are concerned that the proportion of benzene in gasoline, which is unregulated in both Canada and the United States, will consequently increase. The Commission recommends, therefore, that the Government of Canada evaluate the health effects of increased benzene in motor gasoline, and consider establishing limits on the allowable concentration. [TA, pp. 13-18]

4. Methyl cyclopentadienyl manganese tricarbonyl (MMT) is currently allowed as an octane enhancer in all gasolines in Canada, but is prohibited in unleaded fuel in the United States. After considering the evidence summarized in the following technical appraisal, we find that the current-technology catalysts are unlikely to be damaged or rendered inoperative by the use of this compound at the present federal standard concentration (.018 grams of manganese per litre). [TA, p. 7]

5. MMT also has implications for human health. Although highly toxic in its pure form, it does not normally present an occupational handling problem at the very low concentrations used in gasoline. It is almost completely combusted to manganese oxides in the automobile engine, so that the additive itself is not a hazard. The toxicity of manganese to the central nervous system and other organs at very high levels of exposure is well known. So are the effects of manganese deficiency, at the other end of the spectrum. [TA, pp. 6-8].

6. Manganese is one of the more abundant elements in the earth's crust, and its high concentration in soils, water and air reflects this fact. National Health and Welfare Canada has predicted that the average additional individual intake of manganese resulting from the use of MMT in gasoline is likely to be no greater than 0.3 micrograms per day (µg/day). This compares with an average individual uptake from food, water and respiration of about 100-140 µg/day. By comparison with these large amounts already handled by the body, the extra loading on the public at large from MMT is and will remain very small. [TA, pp. 10-11].

7. Methyl tertiary butyl ether (MTBE) is increasingly being used as an octane enhancer in the United States. It is totally miscible with gasoline so that, unlike methanol (from which it is made), it does not require a cosolvent (such as ethanol or tertiary butanol) to prevent it from dissolving in any moisture that may be present in the fuel system and separating out into two liquid phases. The oxidation products of blends of MTBE and gasoline are broadly similar to those of gasoline. [TA, pp. 22-23]

8. The Commission hence concludes that MTBE is safe to use and is an attractive option, though its manufacture implies an energy penalty by comparison with methanol itself. Isobutylene, the other feedstock used in its manufacture, is in short supply in Canada, so that MTBE is likely to be imported, with a negative impact on the balance of payments. Health and environmental problems associated with its use in automotive fuels do not appear to be any greater than those for gasoline. [TA, pp. 22-23]

9. Canada is one of the world's largest producers of methanol, which is the only alcohol additive or alternative fuel that is a viable option for this country. It can be used either as a blend with gasoline, usually at concentrations of 5%, or as an alternative fuel (85-100%). Methanol is itself a toxin, whose oxidation leads to increased emissions of formaldehyde, a toxic compound that is also reported to have carcinogenic properties at high exposure levels. Formaldehyde and methanol emissions can be easily oxidized by catalytic converters, however, and we believe that they do not represent a health hazard at

the low concentrations found in the emissions from methanol or methanol blends. [TA, pp. 23-26]

10. The use of neat methanol fuels involves technologies that can only be factory-fitted at the time of manufacture. Otherwise, corrosion and damage to the fuel system will ensue. The emission catalyst system of such vehicles will be tailored to control the formaldehyde formed. Methanol/gasoline blends, on the other hand, are suited to the existing vehicle fleets. [TA, pp. 28-33]

11. Propane has become fairly popular as an alternative fuel. Although it has been widely used for fleets of delivery vehicles and taxis, we doubt whether it is likely to become a significant alternative to gasoline. Propane-fuelled vehicles appear to be economical to run, but maintenance of these retrofitted gasoline vehicles will probably be costly in the long run, as their fuel systems were never designed to run on propane. Regulated emissions (CO, NO_x, hydrocarbons) are generally lower than for gasoline engines, but there is little information on the health effects of propane, other than that it is an asphyxiant in high concentrations. It is probably safe to assume that emissions are likely to comprise a quite small number of simple compounds, given that the propane molecule has only three carbon atoms, and that the fuel itself is fairly pure and not a mixture of hundreds of compounds as is gasoline. [TA, pp. 33-35]

12. Compressed natural gas is mainly methane. Its oxidation products are predominantly CO, CO_2 and water, with some NO_x and possibly formaldehyde, depending on the fuel-air mixture. Among its main advantages are the direct use of natural gas and the fact that, in

principle, vehicles can be refueled overnight through the domestic and industrial gas distribution system. The radical difference from other fuels makes retrofitting impossible so that the system has to be factory designed and built. We believe that these advantages are outweighed by the need for vehicles to carry high pressure tanks, and the cost and possible danger of operating high-pressure home pumping stations. (TA, pp. 35-36)

TECHNICAL APPRAISAL

by

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TECHNICAL APPRAISAL

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Introduction

In its interim report, Lead in Gasoline: a Review of the Canadian Policy Issue, the Commission reviewed the health concerns and economic effects that arise from the presence of lead in gasoline, and its phasedown (RSC, 1985). During its investigations, the Commission accepted the view that to reduce or eliminate lead from gasoline by switching to lower octane fuels, and to engines with lower compression ratios, was unrealistic. To do so would be both uneconomic and inefficient in terms of fuel consumption. If tetraethyl lead is no longer to be used as an octane enhancer in gasoline, or its role restricted, other octane sources have to be found. The health and environmental impacts of such substitutions have to be evaluated. It would be unwise to substitute another set of problems for those posed by lead. This question is thus within the Commission's terms of reference, even though it does not arise from lead directly.

Fuel octane can be matched to engine compression ratios in several ways or combinations of ways:

(i) more severe refining of petroleum fuels, converting low octane hydrocarbon molecules into differently structured but chemically similar molecules with higher octane values by reforming, cracking, alkylation and isomerization (PACE, 1985);

(ii) replacing tetraethyl lead in the fuel blend with other additives; and

(iii) using different fuels having more satisfactory antiknock and emission characteristics than gasoline.

In considering these options, one has to keep in mind their effect on the very large existing fleet of vehicles. Some may be new car technologies, others may require more or less expensive retrofitting, and yet others may be totally unsuited to the older but still useful car.

The Commission is surprised by the paucity of information on the health and environmental impacts of such changes; indeed, the available evidence deals almost solely with the regulated exhaust constituents--carbon monoxide, unreacted hydrocarbons and oxides of nitrogen--and whether they are within the limits prescribed. Most of the literature relates to the technical aspects of the fuels or blends, including effects on driveability, engine wear and corrosion, catalyst plugging and vapour pressure. Although the toxicity of the actual additives has been examined, there is little information on their combustion products, and the forms in which they reach the environment and target organisms, particularly humans.

Refining

Crude oils are separated by distillation into several progressively heavier fractions, whose properties depend on the size and structures of the different hydrocarbon molecules. These fractions are separated, treated and blended to make a variety of different products, such as gasoline, jet fuels, diesel and furnace oil (PACE, 1985). Generally the lighter (i.e., lower boiling) fractions that contain relatively short molecules (chains of up to 8 carbon atoms) are those used to manufacture gasolines. In order to increase the yield, however, heavier fractions with larger molecules are broken down or cracked into smaller molecules with lower boiling points.

Intermediate refinery products are upgraded into more effective fuels by reforming, a process that typically changes a low octane (60-70) material to about 90 road octane (RON) by increasing the proportion of aromatic hydrocarbons and converting hydrocarbon molecules with straight chains of 8-carbon atoms into molecules with branched chains.

Octane rating can be raised by more severe reforming, but this tends to increase the concentration of the aromatic hydrocarbons in the final product. Aromatic compounds typically constitute 20-35% of the volume of regular unleaded gasoline, and up to 50% of premium gasoline. The aromatics produced are predominantly xylenes and toluene, with smaller amounts of benzene. Several aromatic compounds, including benzene (USDH, 1982), are known carcinogens. Several are toxic. The health effects of these compounds are described below under additives.

All such aromatics increase the vapour pressure, i.e. volatility, of the gasoline blend, increasing evaporative emissions, the level of exposure for workers in service stations, and for the public in self-serve stations (US EPA, 1978 a). Although almost all the aromatic compounds are destroyed in the automobile catalytic converter, small amounts do escape in the emissions, and these quantities will increase with the higher concentration of aromatics in the gasoline. In view of this problem, and the large number of older vehicles without catalytic converters that will be on the roads for at least the next decade, more severe reforming alone does not seem to be a prudent approach to achieving the octane levels required.

Far more satisfactory is isomerization of the front-end naphtha, a low boiling fraction of low octane value, rich in straight chain molecules with predominantly 5 carbon atoms. The branched chain forms (isomers) of these compounds have very high octane values, and the isomerized fraction is blended back to produce a gasoline with the desired characteristics. Conversion requires a special isomerization plant. None has as yet been designed and built to operate in Canada for motor fuel (PACE, 1985), although they are common in the chemical industry, and for isomerizing butane in refineries.

Isomerization appears to be a most attractive option, since the exhaust emissions are those of gasoline. The health implications should be no greater than at present for efficiently functioning catalyst-equipped cars. For older cars, the lead content of gasoline can be reduced to the levels apparently needed to avoid valve recession (Weaver, 1984). The capital cost is high, but the extra cost to the consumer will be quite small (in the order of 1¢ per litre in the retail price of gasoline). The construction of isomerization capacity will also provide a short term boost to the engineering and construction sectors of the economy. As the isomerization plants will operate in Canada using Canadian materials, there will be no long-term drain on the balance of payments (RSC, 1985, pp. 37-45).

A cautionary note must be sounded, however, with respect to <u>all</u> gasoline fuels. A paper on the chronic toxicological properties of gasoline, published recently by the American Petroleum Institute, Exxon Research and Engineering Company and others (MacFarland et al., 1984), indicated that chronic low level inhalation of unleaded gasoline vapour

produced a high level of renal carcinomas and sarcomas in rats, and histopathological examination revealed an increase in liver nodules at higher exposures. There is some evidence that the renotoxic effect of whole gasoline may be due to the presence of one or two of the five main groups of hydrocarbons present in gasoline, iso-alkanes being the most suspect. Work on this project is continuing, and the relevance of the results to human subjects is under active investigation. It should be noted, however, that typical human exposures to the concentrations used in the experiments are much shorter. Nevertheless, if this work is substantiated, the continued use of, or exposure to, gasoline fuels will have to be carefully evaluated.

Additives

Tetraethyl lead has been extensively used as an octane enhancer since the mid 1920's, though it has been progressively phased down since 1974 in North America. Its use in gasoline has led to widespread distribution of lead throughout the human environment (Nriagu, 1985), and its continued use has led to concern about health impacts. Regulations now restrict the use of lead in gasoline; other regulations will require all new light duty vehicles to be equipped with catalytic exhaust converters and use unleaded gasoline. As a result, lead will effectively disappear from fuels by the mid 1990's (RSC, 1985, pp. xiv). Several other additives have been suggested to replace lead as knock preventative and octane enhancer.

Methyl cyclopentadienyl manganese tricarbonyl (MMT) has been used extensively since 1957 as an antiknock replacement for tetraethyl lead. Developed and marketed by Ethyl Corporation, it is currently used in Canada in unleaded fuels (PACE, 1985). It remains in use in the U.S. in leaded gasoline in concentrations that have increased since the reduction of the lead content in that country, although it has been prohibited in unleaded gasoline because it is believed to interfere with effective reduction of exhaust emissions (Benson, 1978; Benson et al., 1979; US EPA, 1978 b, 1984). This does not seem to be the case with current technology vehicles (Shantora et al., 1985); indeed, in eight years of use of MMT in unleaded gasoline in Canada there does not appear to have been a higher incidence of catalytic converter failure than in the United States. MMT does not appear to cause failure of the oxygen sensor or deactivate the catalyst. The converters that were prone to plugging in the 1970's were of the monolithic type, consisting of a ceramic base impregnated with the precious metal catalyst. The pore size of these catalysts was much smaller than the modern pelletized catalysts which prevent the development of engine back-pressure.

The effects of MMT on automotive emissions are very small. They appear to range from slightly improved to slightly worse than for clear unleaded fuel, but it is unlikely that even a fleet test of unprecedented magnitude and scope would be large enough to show any statistically significant differences (Falkiner, 1986). The Canadian General Standards Board (CGSB) is currently reviewing the effects of MMT use on vehicles in Canada, and it expects to complete its study in mid-1986.

MMT itself has been found to be extremely toxic and to require stringent precautions at all stages of manufacturing, transportation and blending with gasoline. It penetrates the skin readily, and its ultimate site of action is the central nervous system. Studies with rats have shown that MMT is rapidly metabolized and distributed to the liver, kidneys and lungs, with the latter showing the greatest immediate toxic effects at low concentations (NHW, 1978). Its concentration in gasoline blends, however, is extremely low (0.072 g/L; 0.018 g Mn/L), so that the primary concern appears to be with its exhaust emissions. MMT is almost completely oxidized (99.7 %), mostly to Mn_3O_4 and MnO, with smaller amounts of other oxides present (Ter Haar et al, 1975). Any uncombusted MMT is rapidly photochemically decomposed.

It has been widely claimed that, as manganese is an essential component of human and animal diet, the anticipated levels of atmospheric manganese should pose no threat to human subjects (NHW, 1978, 1983, 1984; Cooper, 1984; Schroeder et al., 1966). However, this subject cannot be dismissed without investigating the possible accumulation in dusts and soils over extended periods of time, a process that has been responsible for the most intractable aspects of the lead issue.

Unlike lead particles, the manganese oxides that reach the soil are not likely to remain concentrated in the upper few centimetres for any length of time. The pH of the generally moist conditions prevailing in soils will cause mobilization of the manganese, which will move to lower levels and ultimately reach the groundwater or surface waters (Costescu and Hutchinson, 1972). Thus the manganese of gasoline origin actually reaching human populations will indeed be almost exclusively directly inhaled or ingested, in incremental quantities insignificant compared with the normal

exposure through food and respiration (0.3 µg/day additional intake against an uptake of 120 µg/day without MMT) (NHW, 1978; Ethyl Corp., 1985). Average intake of manganese in Canada is about 3600 µg/day from food, 40 µg/day from water and 2 µg/day by direct inhalation.

Manganese and its compounds, particularly the chlorides and oxides, have been extensively studied in recent years, largely because of the fact that high exposures give rise to manganism, a toxic condition of the central nervous system that has symptoms similar to Parkinson's Disease. Ulrich et al. (1979) reviewed the conditions of exposure at which symptoms of manganese intoxication become apparent. They found these to be in excess of six months at levels above 2-11 mg Mn/m^3, although the albumin/globulin ratio was disturbed at six month exposures as low as 0.03 mg/m^3 and some evidence of peribronchial and perivascular sclerosis were noted at 0.3 mg/m^3. Manganese oxides and chlorides administered at higher dosages (up to 400 mg/kg body weight) affected phosphatase metabolism and led to an increase in calcium and degenerated neurons (nerve cells) in rabbits. Similar dosages depleted the dopamine content of the caudate nucleus in monkeys.

Ulrich and his co-workers then designed experiments to observe the effects of chronic exposure similar to those likely to result from internal combustion engines. His exposures were 100 to 10,000 times as much as the normal ambient atmospheric levels of manganese (1.5 $\mu g/m^3$ in the most heavily industrialized manganese-related centres and 0.1 $\mu g/m^3$ in others). They exposed rats and monkeys to levels of 11.6 to 1,152 µg Mn/m^3, generated as an Mn_3O_4 aerosol by burning MMT in propane, and did hematological and serum biochemical and histopathological evaluations at regular intervals. No clinical signs of toxicity were found in any of the

animals, although at the highest levels (1,152 µg/ m^3) accelerated weight gain and slightly elevated hemoglobin were noted, as was some evidence of hypophosphatemia. No histopathological abnormalities were observed. Evaluations of pulmonary function, electromyographic activity, and limb tremor showed no effect; nor did tissue manganese levels change after six months. After nine months exposure, however, reversible elevated manganese was found in kidney, lung, spleen and blood; this was dose related.

The fact that liver manganese showed no increase is consistent with the homeostatic control of manganese metabolism through mitochondria. Manganese accumulates preferentially in tissues rich in mitochondria, but unfortunately, in contrast with the case of lead, little is known of its effects on cell biochemistry following chronic exposure to low levels.

Several papers have appeared describing manganese retention and distribution, many written by EPA scientists in response to the limited information available in the mid-1970's on the toxicity of Mn_3O_4 from MMT exhausts. It is now generally accepted that infant rats retain up to twenty times more manganese than adolescents and adults (Cahill et al., 1980; Kostial et al., 1978) and that manganese accumulation is promoted by iron deficiency in the diet (Lasky et al., 1982; Rehnberg et al., 1982). All the rats used in these experiments were fed manganese at rates in excess of 70 µg/day/g body weight, and as much as 3,550 µg/g, which are much higher than the Canadian average intake for a 70 kg adult (3,600 µg/day, equivalent to 0.05 µg/day/g). At these rather high levels of exposure homeostasis apparently does not occur in young rats before weaning, when blood-brain and blood-testicular barriers to manganese start to be noticeable, and the intestinal wall begins to prevent or control uptake. Elevated manganese concentrations in the brain have been observed

to alter neurotransmitters, and Rehnberg et al. (1981) report that it is strongly absorbed in the cerebrum, hypothalamus and pituitary of pre-weanling rats. As it has a long residence time, these authors conclude that "... the neonate is sensitive to the toxic effects of Mn_3O_4", but no evidence of actual damage is presented.

Rehnberg et al, (1980) have also noted dose-related acceleration of post-natal liver iron depletion, depression of erythrocytes, hematocrit, hemoglobin and body weight and survival; all these experiments were done at manganese dosages between 21 and 214 µg/day. Bird et al. (1984) found that monkeys exposed to excessive (greater than 30 $\mu g/m^3$) manganese dust developed neurological abnormalities resulting from dopamine concentrations, which were related to the quantities inhaled and the period of exposure; but as in all the other work cited, these levels cannot be related to the chronic low level exposures of concern in the gasoline issue.

Barbeau (1986)* has suggested that it may be more important to compare the average additional intake of manganese predicted for MMT use (0.3 µg/day) with the present average intake due to inhalation (2 µg/day), than with the current daily uptake from food and water (100 - 140 µg, according to diet and location). Inhaled manganese will be absorbed in the lungs and some transported directly to the brain, probably exerting a more significant neurological effect than the ingested manganese uptake, which is first metabolized in the liver. These inhalation exposures, however, are two orders of magnitude below the lowest used in Ulrich's (1979) carefully controlled chronic inhalation study on rats (p. 8), at which no histopathological, pulmonary or electromyographic abnormalities were

*We were sorry to hear of Dr Barbeau's death shortly after this discussion.

observed, although Bird (1984) did note the onset of dopamine-related abnormalities over the same general range of exposures.

Parkinson's Disease has been postulated to result from the interplay of environmental factors and individual genetic susceptibilities, against a background of normal ageing. Many potential toxins are detoxified by hydroxylation in the liver by P450 cytochromes. Barbeau and his co-workers (1985) have suggested that people with defective hydroxylation mechanisms may be more susceptible if exposed to environmental neurotoxins and, as a result, develop chronic degenerative disorders like Parkinson's Disease. Manganese is known to be implicated in parkinsonism (Barbeau, 1984; Cotzias, 1958), and Barbeau (1986) has suggested that it may also inhibit hydroxylation by P450 cytochromes. This might be particularly significant in sensitive gasoline station attendants if MMT were to be used.

MMT has already been used, however, for 8 years in unleaded gasoline, which currently comprises about half the gasoline consumed in Canada. The additional exposure to manganese is well within the normal range represented by dietary variations, and is likely to remain so. Aside from the occupational problem related to the possible genetic susceptibility of some workers in gasoline stations, Cooper's view (1984) that the general public has a wide margin of health safety with respect to the worst case use of MMT in gasoline appears to be sound.

Aromatic Hydrocarbons: Benzene, Toluene and Xylenes. Many aromatic hydrocarbons are toxic, and some are carcinogenic to both humans and experimental animals (NHW, 1979; IARC, 1982; Maltoni, 1983; Goldstein, 1983). Of concern is whether their increased use as gasoline additives might pose any hazard to the general public.

Benzene is quite widely used in Europe as an octane enhancer in gasoline, and the European Communities allow a maximum level of 5% in the fuel (CEC, 1985). Benzene is not added to gasolines in North America, and there is no maximum permitted level in Canada or the United States, but the proportion used is generally about 2-3% in the final blend. In some countries it may be as high as 15% (Maltoni, 1983). The reforming process produces large amounts of benzene, toluene and the three molecular forms (isomers) of xylene in the refinery (PACE, 1985). Significantly higher concentrations of aromatic compounds are found in all gasolines refined from tar sands.

Despite the fact that benzene is a good octane enhancer, it commands a high price as a chemical feedstock for the manufacture of plastics, and most of it is removed. The chemical demand for toluene and xylenes is smaller at present and, being quite efficient octane enhancers, they are left in the reformate, constituting between 15 and 20% of the final gasoline blend (Halpern and Noble, 1985). This situation is likely to end abruptly once the disappearance of lead banking allows the full impact of the rapid phasedown of lead in the U.S. to be felt in the marketplace, probably in 1988.

Halpern and Noble (1985) believe that, had the U.S. lead reduction been planned over a period of five years or more, refiners would have had the time to make up the overall pool octane shortage of some 2.5 octane numbers through plant investment in such processes as ultra-high severity reforming, alkylation or isomerization. The rapid phasedown restricted the options open to refiners, allowing them only to increase the reforming severity of their existing plant or to blend in aromatics; industry capacity for the manufacture of MTBE and tertiary-butanol-methanol octane

enhancers is currently inadequate to make up the entire shortfall. Increases in reforming severity will recover about half the octane shortfall, largely by increasing the proportion of aromatics. The remainder will have to come from further aromatic additions.

As aromatics become more valuable and there is increasing competition between the petroleum and chemical industries, their value as octane enhancers will rise relative to that as chemical feedstocks, leading to competition for their supply, and inevitably to higher prices. Furthermore, the limited volume of aromatics that will be available within the U.S. will have little effect on the octane shortfall, so that imports will be needed until the investments in new plant processes can redress the balance in the market (Halpern and Noble, 1985).

Refineries in Canada generally produce gasolines containing about 2% benzene (rarely exceeding 4%). The median total aromatics seems to be in the vicinity of 20%, although a few are already approaching 50% in order to achieve acceptable octane levels (NIPER, 1983). Although Canadian refiners, unlike their U.S. counterparts, are permitted to use MMT in unleaded gasoline, it is not as effective an octane enhancer as tetraethyl lead, and we shall also probably face greatly increased proportions of aromatic hydrocarbons in gasoline.

Aromatic additions increase the vapour pressures of the fuels, leading to evaporative losses to the atmosphere from the fuel system during driving. This fact has already resulted in regulations mandating the venting of carburetors and fuel tanks through canisters filled with activated carbon. Elevated vapour pressures are also responsible for vapour lock in the fuel system and other driveability problems, and to greater exposure to fuels through inhalation and handling in filling

stations (US EPA, 1978 a). Though this might be expected to represent mainly an occupational hazard, the increasing number of self-serve gasoline stations exposes an ever-larger proportion of untrained members of the general public; exposure levels in gasoline stations are similar to industrial exposures (NHW, 1979).

Benzene is known to be both a toxin and a carcinogen; many of its toxic properties were documented during the 19th century, and its carcinogenicity was first reported by Delore and Borgomano (1928). Its main exposure route is through inhalation. The US OSHA (1985) standard is 3.2 mg/m^3 for 8 hours, and the action level is 1.75 mg/m^3. Although levels of 10,000 mg/m^3 can be tolerated for 30 to 60 minutes, acute effects become apparent at exposures above 3,500 mg/m^3. Acute symptoms generally involve the central nervous system--muscle tremors, convulsions and paralytic asphyxiation, which in non-lethal cases can persist for several weeks after the event (NHW, 1979).

Humans absorb about half the benzene inhaled, and retain about 30%, the remainder being exhaled unchanged (NHW, 1979; IARC, 1982). The retained benzene is metabolized mainly in the liver, where it increases lipid peroxidation (Khan et al., 1984), and other lipid-rich sites such as bone marrow where much of the synthesis of blood occurs. Its effects on the hematopoietic system are thus not surprising. The hemotoxicity of chronic exposure mainly results from destruction of the myeloid and erythroid components of the bone marrow, leading ultimately to pancytopenia, in which there are decreases in white blood cells (leucopenia), red cells (anemia) and platelets (thrombocytopenia) (Goldstein, 1983). There is consequently a decrease in the body's ability to resist infections. Blood cell chromosome abnormalities have also been

reported (Snyder, 1984). Little is known of the mechanisms of the processes, but some of the metabolites have been identified with radioactive tracers. The most important are phenol, catechol, quinol and hydroquinol; the specific effects of benzene toxicity are believed to be mediated by benzene epoxide, which is a transient metabolic intermediate (Irons, et al., 1983), although a toxic aldehyde precursor of muronic acid has also been suggested (Gad-El Karin et al., 1985).

These hematological effects have been reported at occupational exposures of 17.5 to 122 mg/m^3 for three months, although they occur more generally at exposures above 350 mg/m^3 (NHW, 1979; Snyder, 1984). Age, sex and familial factors are believed to play a role in individual susceptibility to pancytopenia. Removal of the exposed worker usually results in recovery, although some effects may persist for several years (NHW, 1979; Sato et al., 1975; Aksoy et al., 1974, 1976).

There is strong evidence for a relationship between benzene exposure and some forms of leukemia, although proof of this has been hampered by the lack of an adequate animal model upon which to base a dose-response relationship. Also restrictive are the absence of satisfactory epidemiological data, which are almost impossible to obtain, and the incomplete understanding of the mechanism of induction (NHW, 1979). Other hematological disorders that may be related to benzene exposures are Hodgkin's disease, lymphocytic lymphoma, myeloid fibrosis and multiple myeloma.

Goldstein et al. (1980) observed a few cases of acute and chronic myelogenous leukemia in benzene-exposed rats and mice, and suggested a possible causative effect, but Maltoni (1983) asserted that their data were inadequate. Maltoni was able, however, to use an animal model

satisfactorily to induce zymbal gland carcinomas in rats and demonstrate a dose-response relationship. Goldstein (1983) considers benzene to "... definitely ... be a cause of leukemia in man". He derives his evidence from a number of different approaches, different types of epidemiological studies and many case reports. Goldstein refers to the impressively large numbers of case reports associating benzene with acute myelogenous leukemia and the frequency with which benzene-induced pancytopenia has been followed through a pre-leukemic phase into acute myelogenous leukemia. Table I summarizes Goldstein's view of the current state of knowledge of the relationship of benzene exposure to hematological disorders.

Urban non-occupational exposure of individuals to benzene has been estimated at about 125 mg/yr, of which 90 mg comes from food, but the significance of oral against respiratory uptake cannot be evaluated (NHW, 1979). Ambient air exposure is in the range of a few micrograms per cubic metre, of which 80% owes its origins to gasoline-related emissions, although Weaver et al., (1983) found atmospheric benzene levels in pristine areas to be about 60 $\mu g/m^3$. At the levels encountered in the atmosphere, there is no clinical, experimental or epidemiological evidence that points to demonstrable health effects in humans, but the Department of National Health and Welfare cautions that this chronic exposure is spread over a lifetime, so that there may be some effects, so far unidentified (NHW 1979). Indeed, if there were a major increase in benzene in gasoline, the population exposure to benzene would undoubtedly be much higher than the department estimated in 1979.

Women are especially at risk from benzene due to its high liposolubility, and elimination from the body is likely to be slower due to their higher fat/body weight ratios (Sato, 1975). Their hormonal balances are

Table I

Relationship of benzene exposure to various hematological disorders.

A. Causality Proven

1. Pancytopenia: Aplastic Anemia
2. Acute Myelogenous Leukemia and Variants (Including Acute Myelomonocytic Leukemia, Acute Promyelocytic Leukemia, Erythroleukemia)

B. Causality Suspected

1. Chronic Myelogenous Leukemia
2. Chronic Lymphocytic Leukemia
3. Hodgkin's Disease
4. Paroxysmal Nocturnal Hemoglobinuria

C. Association Suggested But Unproven

1. Acute Lymphoblastic Leukemia
2. Myelofibrosis and Myeloid Metaplasia
3. Lymphoma: Lymphocytic, Histiocytic
4. Thrombocythemia

Source: Goldstein, 1983

also likely to be more severely affected (NHW, 1979). The placenta is not a barrier to volatile solvents, but fetal exposures to levels not toxic to the mother do not appear to produce teratogenic effects (Lee et al., 1983).

Many aromatic hydrocarbons have been shown to be carcinogenic to animals, and some to humans (USDH, 1982). The group of polyaromatic hydrocarbons (PAH) is particularly dangerous, but they are present in gasoline exhaust emissions in only minuscule quantities. The most significant of these compounds is benzo-α-pyrene, which may constitute as much as 0.0003% of the exhaust gas; PAH's are, however, of greater concern in diesel exhausts. Most of the benzene and other aromatic hydrocarbons in gasoline are undoubtedly oxidized and destroyed during the combustion process and the subsequent catalytic conversion of the exhaust gases (Nebel, 1979), although some benzene is actually produced in the fuel combination process from precursors present (Black et al., 1980). The extent to which unconverted aromatics escape, especially through malfunctioning converters, remains uncertain and is masked by emission standards that generally refer to total hydrocarbons and do not discriminate further. Black et al. (1980), however, found that as total hydrocarbon emissions were reduced, the proportion of paraffins in the exhaust increased; i.e., the proportions of aromatics decreased. This implies a more efficient removal of aromatics from the exhaust gas than paraffins.

Some recent work on benzene emissions corroborates this assertion (Seizinger et al., 1986). Two groups of fuels were made, one containing 25% aromatics, and the other with 40%. Each group comprised three fuels in which the benzene concentrations were 0.03%, 1.5%, and 4%. Unfortunately, the individual concentrations for the other aromatic hydrocarbons in the

fuels were not specified. The exhaust and evaporative emissions of benzene and total hydrocarbons were measured, and are here expressed in grams per kilometre driven. Only exhaust emissions are, of course, quoted for CO and NO_x. Increasing benzene concentration led to a small increase in benzene exhaust emissions, although total hydrocarbons decreased slightly. The combustion process and the catalyst were seen to be remarkably efficient in removing benzene; a 100-fold increase in the concentration of benzene in the fuel, together with some small amount of benzene actually formed during the combustion process, resulted in less than doubled benzene exhaust emissions. For the 25% aromatic base fuels the measured benzene exhaust emissions increased from 5.0 mg/km to 8.7 mg/km, and hydrocarbons decreased from 0.22 g/km to 0.18 g/km. For the 40% base aromatic fuel, hydrocarbons showed no change with benzene concentration. Evaporative emissions for benzene showed little difference with concentration but hydrocarbons are distinctly lower in the 40% aromatic base fuels.

The health effects of toluene and xylene have been reviewed for the Department of National Health and Welfare (NHW, 1985) and by the US Environmental Protection Agency (1980). Toluene is the most abundant aromatic hydrocarbon contaminant in air, the average concentrations of toluene, o-xylene, m-xylene and p-xylene in the Los Angeles Basin being respectively 151, 38, 76 and 28 $\mu g/m^3$. Pilar and Graydon (1973) showed atmospheric toluene and benzene contamination in Toronto to be closely linked with automotive traffic density. All these aromatics have been found in Canadian drinking water, generally in microgram per litre concentrations.

The main route of exposure of populations to toluene is by inhalation, with smaller quantities ingested through water. Exposure of Canadians is

estimated to be about 2.3 mg/person/day on average; the worst situation is in Toronto (141 mg/person/day). Mean xylene exposure is about 0.95 mg/person/day. About 40% of the intake of these compounds is immediately exhaled and between 70% and 90% of the amount retained is rapidly metabolized and eliminated, with between 3% and 20% exhaled unchanged.

Inhaled toluene is rapidly transported by the blood to lipid tissues but ingested toluene has first to be metabolized by the liver before reaching the central nervous system. Toluene is metabolized by a mixed function oxidase system to benzyl alcohol, which is oxidized in turn to benzaldehyde and benzoic acid and then conjugated with glycine to form hippuric acid; about 80% of the toluene retained is excreted in this form in the urine within 24 hours. Xylenes behave in much the same way, 95% being excreted as methylhippuric acid. The only danger of accumulation seems to be in adipose tissues on repeated exposure.

Extremely large doses (1 g/kg body weight) are required to show mutagenic effects such as chromosome damage in rat bone marrow. In vitro studies on humans showed no evidence of mutagenicity; no significiant chromosomal aberration was detected in workers exposed to toluene, some exposures being as high as 200 ppm for 15 years.

There have been few studies on carcinogenicity of these toluene-derived compounds. Though they are not themselves carcinogenic, they may be co-carcinogens when inhaled. Exposure to toluene at 300 ppm for 24 months produced no increased neoplastic, proliferative or degenerative lesions in rat organs, and there are no indications that xylene is carcinogenic in animals. In humans, occupational exposure to aromatic hydrocarbon solvents has been linked with lymphatic leukemia, but this cannot be related to any one of these compounds.

Toluene and xylene have been reported to have some teratogenic effects when administered to rats and mice in very large doses--about 0.2 - 0.7 g/kg body weight, and on inhalation at 1 g/m^3. Both are considered to be slightly to moderately toxic, with LD_{50} values for rats ranging from 3.5 to 5 g/kg. These large doses generally affect the central nervous system, leading to dose-related alterations, such as fatigue, confusion, headache and nausea. All have narcotic effects and cause eye irritation. Recovery is quite rapid on termination of exposure. An investigation of rats showed no effects in blood, urine or tissue samples between 30 and 1,000 ppm of toluene vapour; some adverse central nervous system disorders and serum cholinesterase irregularities were noted in rats exposed to xylene vapour (15 mg/m^3) for 85 days.

Emissions from cars fitted with efficient catalytic converters will be low, given the low levels of observed total hydrocarbons. Without reliable information on the toxicity and carcinogenicity of toluene and the xylenes at the very low ambient concentrations likely to be experienced, it is difficult to assess the health risk faced by the population, although it is almost certain to be low. Nevertheless, in the face of possible increases in the aromatic hydrocarbon contents of severely reformed unleaded fuels, it would surely be prudent to regulate the level of benzene and minimize the presence of other aromatic compounds in gasoline. The presence of aromatic hydrocarbons--particularly polyaromatics (PAH's)--in diesel fuels and exhausts is also a matter of great concern that should be further investigated.

Methyl Tertiary Butyl Ether (MTBE). Use of this octane enhancer at concentrations up to 7% in unleaded gasoline is allowed in the United States under an EPA waiver granted in 1979 (EPA, 1979). MTBE is made from methanol and isobutylene (Chase & Woods, 1979), and is totally miscible with gasoline, since it has similar physical properties to the alkanes. The refining industry has seen this as a way of increasing octane by adding a methanol group to gasoline without having to use a cosolvent (Penny, 1983) although its manufacture imposes a substantial energy penalty (Colledge, 1986; COFA, 1985).

In one evaluation, the fuel properties of MTBE and MTBE-gasoline blends were examined, and engine studies showed power output and energy efficiency to be virtually the same as for gasoline fuels (Johnson and Taniguchi, 1978). Exhaust emission tests showed CO to decrease substantially with increasing MTBE, and NO_x to increase somewhat, while hydrocarbon emissions were essentially unchanged. Furey and King (1980) found that when evaporative emissions were reduced by a closed loop carburetor, there was little difference between emissions from MTBE blend and gasoline; without the closed loop, MTBE blend emissions were lower. Aldehyde emissions increased slightly, depending on the fuel/air ratio.

Investigators concerned with safety and toxicological aspects of MTBE have found that MTBE is "...no worse than gasoline" in terms of effects due to inhalation, ingestion or skin absorption (Reynolds et al., 1974) and that it "... is relatively unreactive in the atmosphere, with little tendency to form O_3". Evaporative emissions for 15% MTBE gasoline blends may be as much as 15% higher than for gasoline, while cold start driveability is worse than for gasoline (Furey and King, 1980). No exhaustive study of the toxicology of MTBE or its combustion products

appears to have been undertaken, but it could have a positive health effect by obviating the need for severe reforming with its consequence of increased benzene and other aromatic hydrocarbons.

Major investments have recently been made in Saudi Arabia, Finland, Italy and Ireland to manufacture MTBE (Oil and Gas Journal, 1984; Hydrocarbon Processing, 1984; Chemistry in Britain, 1985; European Chemical News, 1984). Although Canada is one of the world's largest producers and exporters of methanol from natural gas, isobutylene is in short supply in this country, particularly in western Canada where most methanol is made, and the manufacture of MTBE may not prove to be economically feasible with present technology. If MTBE is used to replace lead antiknock agents, it is likely to be imported, which fact, for the large quantities foreseen (up to 15% of the total volume of gasoline consumed in Canada), will have a significant negative impact on the balance of payments.

Alcohols. The use of alcohols as blends with gasoline or as alternative fuels has been the focus of a great deal of discussion in recent years. The possibility of reducing dependence on imported oil while at the same time producing feedstock from renewable (i.e., agriculturally produced) biomass has attracted the attention of government and populace alike. Alcohol blends are extensively used in many countries--ethanol in Brazil, gasohols (gasoline/alcohol mixtures) in many parts of the United States, methanol in Germany. One supplier is marketing an ethanol blend in Manitoba, a methanol-ethanol blend in Saskatchewan, and plans to extend the sale of the latter into Alberta. Another major petroleum marketer is test-marketing a methanol-butanol blend in Ontario.

The House of Commons Standing Committee on National Resources and Public Works is currently considering the implications of widespread use of alcohol fuels in Canada. For Canada, the options appear to be:

(1) gasoline/methanol blends with ethanol or TBA as cosolvent--Canada is one of the world's largest producers of methanol from natural gas and has surplus capacity; and

(2) neat methanol, which is really an alternative fuel, and is discussed later (see section on alternative fuels).

There is an extensive literature on the technical problems of using methanol blends (5 % methanol) in engines and systems designed for gasoline (MVMA, 1985). These range from corrosive effects on the terne plate of gasoline tanks, to chemical reactions with engine components and hoses, particularly plastics. Methanol is more soluble in water than in gasoline and, unless a cosolvent such as ethanol or t-butanol is used, the absorbed moisture can cause separation into two liquid phases (gasoline and a methanol-water solution), with disastrous results for fuel combustion, efficiency and driveability.

Methanol, if simply added to normal gasoline, would produce a higher fuel vapour pressure than gasoline blended in accordance with Canadian General Standards Board specifications. Refiners who use methanol in gasoline blends must compensate for the higher vapour pressure of methanol by removing some of the lighter hydrocarbons, mainly butane, that are normally blended into gasoline. Butane is a low cost, relatively high octane hydrocarbon with higher energy content than methanol. The substitution of methanol for butane, therefore, carries a levered economic debit that reduces the apparent octane cost advantage of methanol. In

provinces where gasoline does not have to meet the CGSB vapour pressure specification, methanol blends may become more attractive.

Switching between different blends or between blends and straight gasoline poses problems for existing vehicles. Though some of the automotive manufacturers have produced experimental engines that can cope with switching throughout the entire range between gasoline and neat methanol by using modified fuel injection systems, this is essentially new car technology and therefore a longer-term option (MVMA, 1985). Almost all the literature on alcohol/gasoline blends relates to their use and effectiveness in conventional vehicles. Some papers and reports deal with the emissions of regulated pollutants (CO, hydrocarbons and NO_x). Only a few are concerned with non-regulated emissions (primarily aldehydes), and not one was found to deal extensively with the health implications of widespread use of alcohols as or in automotive fuels.

There do not, however, appear to be significant differences in the composition of the unburned hydrocarbon emissions between methanol blends and the unblended gasoline-- n-butane, toluene, iso-pentane and other volatile gasoline constituents that dominate the exhaust emissions (Gabele et al., 1985).

Others have drawn attention to the importance of the air-fuel ratio in achieving low emissions with alcohol blends (MVMA, 1985; Wathne and Hov, 1985). Where the activated carbon canister used to prevent evaporative emissions from the fuel system and the carburetor fails (canister break-through), n-butane comprised about 70% of the total evaporative emissions, compared with 25% otherwise (Gabele et al., 1985). Only barely detectable quantities of methanol were present in a relatively small percentage (15%) of Gabele's tests on blended fuel. The blends used in the research,

however, tended to have higher vapour pressures than the straight gasolines as they were simply mixed and not blended, and the volatile butane content was not reduced (or backed out) to conform to any particular specification.

In methanol blends, carbon monoxide and hydrocarbon emissions are found to be generally much the same as for straight gasolines, while oxides of nitrogen are somewhat lower (Gabele, 1985). Methanol is, however, a primary alcohol, and like all members of this group, is oxidized to form an aldehyde, in this case formaldehyde; similarly, using ethanol as cosolvent would lead to acetaldelyde as well. Aldehyde emissions are indeed found to be some 50% higher with the blends than for straight gasolines (Gabele, 1985), but the amounts involved are extremely small and they are quite efficiently removed by the catalysts, so that the possibility of negative health effects appears to be remote. The aldehyde situation for neat methanol fuels (85-90% methanol) is somewhat different (see below).

Alcohol blends present an attractive health and environmental alternative to the increase of aromatic hydrocarbons resulting from severe reforming.

Alternative Fuels

Six practical fuel systems exist for automotive propulsion: gasoline, diesel, alcohols (neat methanol in Canada), propane, compressed natural gas (methane), and electricity. All have advantages and disadvantages, and some have limitations that at present restrict their use to specific types of vehicles and functions. The massive world-wide investment in the manufacture and use of traditional gasoline vehicles is a powerful determinant of the economics of alternative power systems. The success of

these vehicles was for many years responsible, in large measure, for the lack of interest in research and development on alternative power systems--high energy-density batteries, for example. It is therefore not surprising that four out of the five alternatives to gasoline are themselves products of the petroleum and gas industries, and that these are the ones that require the least radical technological changes to the conventional gasoline propulsion system.

After a brief spell of popularity for light vehicles following the oil supply problems of the mid-70's, diesel fuel is once again used almost exclusively in heavy duty vehicles and cannot really be considered a replacement for gasoline. Were it ever to regain widespread popularity for light vehicle use, the health and environmental impacts of its aromatic hydrocarbon and particulate emissions would have to be carefully assessed.

Electric propulsion will remain a viable option only for fleets of short-haul local delivery vehicles large enough to carry the heavy lead-acid batteries that are presently the only practicable power source (Energy Ontario, 1982). This situation will not change until some of the recent exciting results of research in new, lightweight high energy-density systems can be developed into usable technologies. Electric systems are certainly the most benign from both environmental and health points of view because almost all the emissions are shifted from mobile to more easily controllable stationary sources--the power station providing off-peak electricity to recharge batteries in the home. Substantial use of electric power is unfortunately unlikely for many years.

Methanol as a Fuel. Canada is one of the world's largest producers of methanol and probably its largest exporter; only 14% of the production is actually used in this country (COFA, 1985). It is produced mainly in Alberta from natural gas, although there are also plants in Quebec. As new plants have come on stream in recent years, mainly in third world countries with low wage-cost structures and, more importantly, artificial exchange rates, the manufacturers are threatened by world oversupply and are seeking to expand the domestic market. The three automotive fuel options open to them are :

(i) gasoline blending, using ethanol or tertiary butanol as a cosolvent;

(ii) conversion to methyl tertiary butyl ether (MTBE);

(iii) using neat methanol.

From the manufacturers' point of view, neat methanol (90-95% methanol with 5 or 10% gasoline) is the preferred option as it does not requre a cosolvent, and it has the potential for the greatest sales volume. Production of MTBE for use as a gasoline additive is less attractive ecomomically due to the shortage of isobutylene, the other essential feedstock, in Western Canada. The Motor Vehicle Manufacturers Association (1985), in a brief to the House of Commons Standing Committee on National Resources and Public Works, recently clearly expressed their preference for neat methanol over blends as a third fuel option, complementary to gasoline and diesel. The MVMA views blends as being of value only in an interim period while substantial numbers of older cars are still on the roads, and then only under strict specification, as many of the methanol blend problems have resulted from inappropriate components or proportions. Neat

methanol fuel requires new car technology. The existing fleet of vehicles was designed and built for gasoline, and many of the materials used are corroded by or unsuited to methanol. Design changes involve, inter alia, modified fuel injection systems and catalytic converters that will cope with emissions of methanol and its oxidation product formaldehyde, both of which are toxic.

Unlike gasoline, methanol combustion produces quite low levels of hydrocarbons, which are now regulated primarily for their role in the production of ozone, a powerful photochemical oxidant (Haagen-Smit, 1952). Methanol fuels do produce emissions with quite high levels of unburned methanol, which is not photochemically reactive, and about ten times more formaldehyde than is the case for gasoline (Gabele, 1985). Although formaldehyde is photochemically reactive, the quantities are very small, so that methanol fuels contribute less to the oxidant problem than does gasoline (Carey, 1981). Overall, however, the emissions of methanol and formaldehyde are together more or less equivalent to the hydrocarbon emissions from gasoline, and methanol produces about the same amount of carbon monoxide. Nitrogen oxides emissions are substantially lower for methanol (Wathne and Hov, 1985), and these could be reduced even further using three-way catalysts; alternatively, the reduction catalyst might be eliminated (Wilson, 1984).

The US EPA (Harvey, et al., 1984) has used a model developed by the Southwest Research Institute to relate methanol and formaldehyde emissions (in grams and milligrams per mile, respectively) to equivalent ambient concentrations (in grams per cubic metre), under typical and severe road traffic conditions in street canyons, roadway tunnels, expressways and garages. These are then related to a range of concern identified from what

they call "... known toxicological and health effects" in order to define a set of design targets. These effects are taken from the literature on occupational health and safety and relate to the onset of clinically identifiable symptoms, such as irritations of the eyes, ear, nose, throat and skin as the lower limit for formaldehyde (0.03 mg/m^3). For methanol, the lower limit is 4.5 mg/m^3, the level at which dilation of the pupil of the eye in response to darkness is sensibly affected.

When actual emission measurements are compared with the equivalent ambient concentrations derived from the model (Harvey et al., 1984), only severe conditions in roadway tunnels would exceed the lower limit of concern for formaldehyde (0.03 mg/m^3), although garages might pose problems, especially in winter. Methanol emissions would not exceed the lower limit of concern (4.5 mg/m^3) under moving traffic conditions, but severe situations in garages would be above the limit. Vehicles with malfunctioning catalytic converters would only exceed the lower methanol limit in the severe roadway tunnel situation, but might exceed the intermediate point for formaldehyde (0.15 mg/m^3) under these conditions. No emissions are likely even to approach the upper limits of concern, which were chosen as the U.S. Occupational Safety and Health Administration proposed standards for workplace exposure--260 mg/m^3 for methanol and 1.3 mg/m^3 for formaldehyde).

Levels of formaldehyde in both personal garages and parking garages would have little effect on the user as exposures would be for short periods--generally only a few minutes; but workers in the building might well be subject to some degree of risk. The same might apply to children living in the vicinity of service stations and parking garages (Ontario

Ministy of Health, 1985). This work has been corroborated by Kraft and Kuhler (1985), who developed a similar model in Germany.

The toxic properties of methanol are well known, and it would have to be denatured, probably by adding 5-10% gasoline before it could be widely sold (Wathne and Hov, 1985). If ingested, it causes permanent damage to the central nervous system, usually blindness, and is often fatal. Little is known about low level chronic exposure, except that it appears to be mediated through formaldehyde by a liver oxidase enzyme. It is interesting that the first clinically noticeable effect should be on the eye at occupational exposures of 4.5 mg/m^3, but is not known whether the reduced ability of the pupil to adapt to darkness and changes in cerebral cortex reflex activity (noted at 1.2 - 1.5 mg/m^3) does in fact represent adverse physiological effects. What is clear, however, is that there are effects of methanol on the central nervous system at levels well below the occupational Threshold Limit Values (TLV).

The background ambient concentration of formaldehyde is approximately 0.1 - 0.5 $\mu g/m^3$, measured at sea and in other remote areas. It is produced by natural processes, such as atmospheric photochemical reactions, and from anthropogenic sources, mainly combustion processes. Formaldehyde makes up between 50% and 80% of all atmospheric aldehydes (Wathne and Hov, 1983). In the atmosphere it decomposes rapidly, so that it is not transported over long distances. Formaldehyde is a toxic compound suspected to have carcinogenic properties; its effect on human health at elevated exposure levels have been well described. Unfortunately the few studies of chronic long term exposure have been marred by uncertainties introduced by the presence of other air pollutants (Meek, et al., 1985).

Formaldehyde is a powerful irritant of the upper respiratory tract, particularly the nose and throat at concentrations in air as low as 1 - 2 mg/m^3; it has also been observed to halt all ciliary movement in the air passages of guinea pigs at this level. Formaldehyde is absorbed through the nasal mucosa, and on ingestion it has been reported to spread through the entire bodies of rats and mice within 5 minutes (Buss et al., 1964). The eye is particularly sensitive, with irritation reported at levels as low as 0.012 mg/m^3, and dose-response relationships measured down to 0.36 mg/m^3. It is classed as a strong allergen but, although cases of asthma and asthmatic bronchitis have been reported, allergic dermatitis is a more common reaction to formaldehyde sensitization (Wathne and Hov, 1985).

Although the Ames test for genetic mutation has shown no effect on Salmonella typhimurium, the bacterium used as a reference (Wathne and Hov, 1985), experiments with human cells in vitro have shown formaldehyde damage to human cells. Mutagenic effects have been reported on yeasts, bacteria, plants and insects (Magana-Schwencke et al., 1978). Formaldehyde is therefore classified as a weak mutagen. No teratogenic effects have been positively identified.

Suspicion of formaldehyde's carcinogenicity rests on exposure of rats and mice at concentrations down to 0.25 mg/m^3 for 24 months. Two out of 235 rats developed nasal carcinomas at 7.4 mg/m^3, and 103 out of 232 developed carcinomas at 18.5 mg/m^3. No cases were observed among rats at 2.5 mg/m^3. Only 2 mice developed neoplasms even at the highest exposures (Swenberg et al., 1980). The interpretations have been strongly criticized as the condition may have been precipitated by chronic tissue changes resulting from nasal lesions (Wathne and Hov, 1985). Despite several reports of possible formaldehyde-induced nasal and lung malignancies, the

results do not provide an adequate basis for asssessing cancer risks. Nevertheless, the U.S. Occupational Safety and Health Administration (1985) has recently promulgated two proposed occupational exposure standards, 2.0 mg/m^3 as an irritant, and 1.3 mg/m^3 as a carcinogen, based on a daily 8 hour exposure. The intervention levels are 1.0 mg/m^3 and 0.67 mg/m^3 respectively.

There is thus need for research to identify the potential effects of methanol and formaldehyde at the low levels to which the public may become exposed before major investments are made in the production of neat methanol fuels and cars.

Propane-Fuelled Vehicles have long been used for short haul specialized purposes, such as fork-lift trucks, as well as stationary power sources. Unlike gasoline, which contains some 400 constituents, the fuel is almost pure propane. Its low cost has made propane-fuelled cars and trucks increasingly popular in recent years as taxis and local delivery vehicles. Fleet owners often maintain their own fuel filling stations, particularly in areas where bulk propane is not widely used. Low crude oil prices provided little incentive for vehicle manufacturers to develop engines suited to alternative fuels, so that conversion from gasoline to propane has been left to propane equipment manufacturers and aftermarket retrofitters. Propane-fuelled vehicles are generally retrofitted gasoline models that were not originally designed to run on this fuel, a situation that voids the manufacturer's warranty. The conversion industry is dominated by small firms, and there have been several reports of fly-by-night operators.

For optimum results, the engine should be designed with the fuel in mind, so that the buyer cannot expect comparable durability and performance from a modified version running on an alternative fuel. Drivers seem to be enthusiastic about propane-fuelled vehicles' apparent economy of operation, but there are many serious problems related to their operation. These have been reviewed for the Transportation Development Centre by Chrysler Canada Ltd. (Lacy et al., 1984).

Propane engines use rather simple carburetors based on the gasoline carburetor design. These are far from optimum with regard to fuel economy, power output and driveability. Unfortunately, good cylinder to cylinder fuel distribution is not assured by feeding in the propane as a gas, using the technology borrowed from gasoline for liquid fuels. The air/fuel ratios are critical to satisfactory operation, and the orifice temperature and pressure have to be carefully balanced against the exhaust manifold pressure to avoid knock. This has to be set mechanically, which is difficult for the often ill-equipped small retrofitter, so it is set at one point, usually 2,000 rpm. This produces high temperatures under other operating engine conditions, which in turn leads to rates of valve recession greater by a factor of 5 to 10 than is the case for an engine designed for unleaded gasoline. Unlike gasoline engines, spark knock occurs at higher engine speeds, where the sound is masked by other engine noise and thus cannot be corrected before damage occurs. The best retrofit systems are deficient at temperatures below $-15^{o}C$, and some even at $0^{o}C$, although a block heater can extend the practical limit to $-40^{o}C$.

Exhaust emissions have lower levels of hydrocarbons and carbon monoxide than do gasoline, but higher oxides of nitrogen, perhaps on account of the higher operating temperatures. They do not use catalytic converters,

although some of the major car manufacturers believe that they should be fitted.

Propane is continuously vented to the atmosphere during refuelling, losing about 50 g per fill-up, typically twice a day for a taxi. Propane vehicles now account for only about 10% of the new fleet, but, since they tend to be heavily used, they probably emit as much total hydrocarbons as the rest of the fleet. There are currently about 125,000 propane-fuelled vehicles in the major metropolitan centres of Canada. The authors of the report believe that concerns about propane safety stem from unfamiliarity, and that they are safer than gasoline powered vehicles in crash situations. (Lacy et al., 1984).

Regulated emissions (carbon monoxide, hydrocarbons and oxides of nitrogen) are lower for propane than for gasoline. Unlike gasoline, these emissions are almost constant at temperatures above $0^{o}C$, but they tend to rise at lower temperatures. Carbon monoxide emissions are particularly low; hence propane's popularity as the fuel for fork-lifts intended for indoor use. There is little information on exposure to propane, other than the comment that it is an asphyxiant that excludes oxygen from the lungs. Once again, there are no details on the health effects of long term chronic exposures, nor of unregulated combustion products in the exhaust. So that its presence in air can be easily detected, small amounts of mercaptans are added. These are mildly toxic sulphur compounds with offensive odours.

Compressed Natural Gas (CNG) has both advantages and disadvantages when used as an automotive fuel. It would be both cheap and easily available, as well as providing a market for natural gas, especially during the summer months. Because it is a gas at ordinary temperatures and

pressures, it must be contained under pressure in the vehicle, necessitating heavy storage containers that require care in replenishing. Ideally, vehicles could be connected to household (low pressure) natural gas supplies overnight and pumped into the car storage bottles overnight; conventional filling stations would find it difficult to pump the gas to high enough pressures sufficiently fast to avoid massive line-ups., The capital cost of a single compressor station is high (about $250,000), so that this technology is better-suited to fleets, bringing it into competition with propane.

One advantage is that it is a new car technology. Retrofitting is not practicable, given the high pressures involved, which require computer control of feed and ignition. On the other hand, it is more difficult to ignite the fuel because its oxidation involves breaking the strong bond between the carbon and hydrogen atoms in the methane molecule. This ignition problem will probably require a dual fuel system to start the engine. There is also a 10-30% loss of power inherent in the system due to displaced volume of the storage containers. Exhaust emissions appear to be similar to those for propane (Lacy et al. 1984).

Some more or less experimental fleets are in operation but widespread use of CNG is a longer term option. However, the weight problem currently is no worse than that of electric vehicles, and if high energy density batteries can be developed in a reasonable period of time, electricity would unquestionably be the safer and cleaner option.

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APPENDIX 6

HEALTH AND MEDICAL RESEARCH COUNCIL

COMMONWEALTH OF AUSTRALIA

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In reply please quote: GJM:JMP
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Dr Keith Wilson
39 Bellevue Drive
BELLEVUE HEIGHTS SA 5050

Dear Dr Wilson

As you requested by telephone, I am writing to pass on to you the outcome of the Public Health Committee's consideration of MMT at its meeting in Canberra on 3/4 September 1987.

In general, the decision was that there were no toxicological concerns over the use of MMT in petrol, but that the matter should be cleared through the Air Quality Committee in terms of vehicle emissions. This was to be expedited after the PHC meeting in order to resolve the matter as soon as possible.

Yours sincerely

DR G J MURPHY
SECRETARY
PUBLIC HEALTH COMMITTEE

15 October 1987

APPENDIX 7

ATTACHMENT 1

INSTITUTE FOR BASIC RESEARCH
IN DEVELOPMENTAL DISABILITIES

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Henry M. Wisniewski, M.D., Ph.D., Director
Peter M. Vietze, Ph.D., Deputy Director

JUL 12 1990

July 6, 1990

Donald R. Lynam, Ph.D., CIH, PE
Director, Air Conservation and
Industrial Hygiene
Ethyl Corporation
Ethyl Tower
451 Florida Street
Baton Rouge, LA 70801

Dear Don:

Thank you for the transcript of the hearing on the manganese (Mn) additive and the copies of comments and studies submitted by various persons regarding potential health affects of exposures to Mn. Based on what I heard at the public hearing and my review of these materials, I would like to make the following comments.

First, as you know, the study of miners exposed to chronic manganese overload revealed that many showed extrapyramidal symptoms including bradykinesia, postural difficulties, prominent rigidity, tremor and, occasionally, significant dystonia. In addition, psychiatric symptoms, referred to as "locura manganica" or manganese madness, were also typically observed. Taken together these data indicate that, in high doses, Mn is a neurotoxic atom. There is no evidence that these effects could occur at levels in the ambient atmosphere. To the best of my knowledge there is no evidence, and none has been cited, that established that children and pregnant women are more susceptible to manganese than males and non-pregnant females.

A questions was also raised regarding the impact of Mn on neurotransmitters. The type of changes in neurotransmitters involved in movement disorders are not clearly understood. Experimental data from various animal species indicate that Mn affects the neurotransmitters that, in humans, are disturbed in Parkinson's disease. For obvious reasons, such studies cannot be done on humans. However, signs and symptoms observed in miners exposed to Mn at high levels indicate that these neurotransmitters are affected

in Mn-induced movement disorders. To my knowledge, there is no evidence to suggest that similar effects take place at lower Mn exposure levels.

I also concur with A. Barbeau's opinion (Neurotoxicology 5(1): 13-36, 1984) that chronic manganese intoxication is not the cause of a form of idiopathic Parkinson's disease. However, Mn can cause a PD-like syndrome, as shown in those studies examining chronic Mn overload.

Regarding the effect of Mn on the immune system, experimental data seem to support the hypothesis that Mn may affect the immune system, at higher levels. These data, however, are not conclusive. In humans, there are no good data to support this hypothesis. And there is no evidence that exposure to environmental levels of Mn (approximately 0.04 ug/m^3) affects human negatively. It is well documented that presently Mn exposure from food and water (3,000 ug/day) is much bigger than from air (0.04 ug/m^3).

During the EPA hearing, Ms. E. Silbergeld's main line of attack was: Ethyl added lead to gasoline in 1925 and this proved to be a powerful neurotoxic atom; today, Ethyl wants to add another metal. Today, in contrast to 1925, we know quite a lot about trace metals' effect on human health. In addition, we also have the EPA, EDF, and other state and city Agencies to monitor the environment. Based on Canadian experience and extensive research (e.g., the Health Effects Institute report on "Potential Health Effects of Manganese in Emissions from Trap-Equipped Diesel Vehicles"), there is no indication that additional manganese from the use of fuel additives will create health problems. According to the HEI report "under the worse-case assumptions, the contribution of manganese from automobile exhaust is not anticipated to be greater than 2.5 percent of the dietary intake. This small contribution of manganese from mobile sources is not expected to tax the homeostatic mechanisms that regulate the levels of manganese throughout the body's tissues." The contribution of Mn from use of the additive would be much less than that examined in the HEI report.

Dr. Donaldson's data on the mechanism of action of Mn are quite interesting but, in my opinion, not relevant to Ethyl's application. The statements by Mr. Hodges and some of those by Dr. Donaldson concentrated primarily on high risk or selective susceptibility cases. Because Mn is an ubiquitous atom and its daily intake is high, to the extent that the people have difficulty in handling Mn, they will develop problems irrespective of Ethyl adding Mn to its products. It will be particularly true if some of the conditions are genetically determined.

In summary, in my judgment, Ethyl provided enough evidence to show that adding Mn to their products will not negatively affect human life and the environment.
While further research is always possible with respect to extremely low level exposures to substances such as Mn, and indeed several interesting avenues for research have been